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## Contents

Does the Greater Understanding of Man and Nature Increase the  
Scientist's Social Responsibility? *A. J. Carlson* ..... 701

Edwin Grant Conklin: 1863-1952: *E. Newton Harvey* ..... 703

## News and Notes

Federation of American Societies for Experimental Biology:  
*M. O. Lee* ..... 705

## Technical Papers

Propagation of Group A Coxsackie Viruses in Denervated Adult  
Mouse Muscle: *Wallace P. Rowe* ..... 710

Catalase Assay with Special Reference to Manometric Methods:  
*Roland F. Beers, Jr., and Irwin W. Sizer* ..... 710

A Quantitative Amino Acid Analysis of Sheep Adrenocorticotropic  
(ACTH) Protein: *Richard M. Mendenhall* ..... 713

P<sup>32</sup> Distribution in the Serum Proteins of the Chicken:  
*R. E. Clegg and R. E. Hein* ..... 714

Degradation of Glucose: *C. T. Bishop* ..... 715

The Adaptation of the Voges-Proskauer Reaction for the  
Quantitative Assay of Streptomycin: *J. J. Szafir*  
and *E. O. Bennett* ..... 717

Liver Function and Bromsulphalein Disappearance:  
*Robert L. Evans* ..... 718

The Influence of Iodoacetate on the Sodium and Potassium  
Content of *Ulva lactuca* and the Prevention of Its Influence  
by Light: *George T. Scott and Hugh R. Hayward* ..... 719

## Association Affairs

Southwestern Division Meeting: *Frank E. E. Germann* ..... 721

Scientific Book Register ..... 722

Twelfth Congress of the  
International Association of Limnologists ..... 3

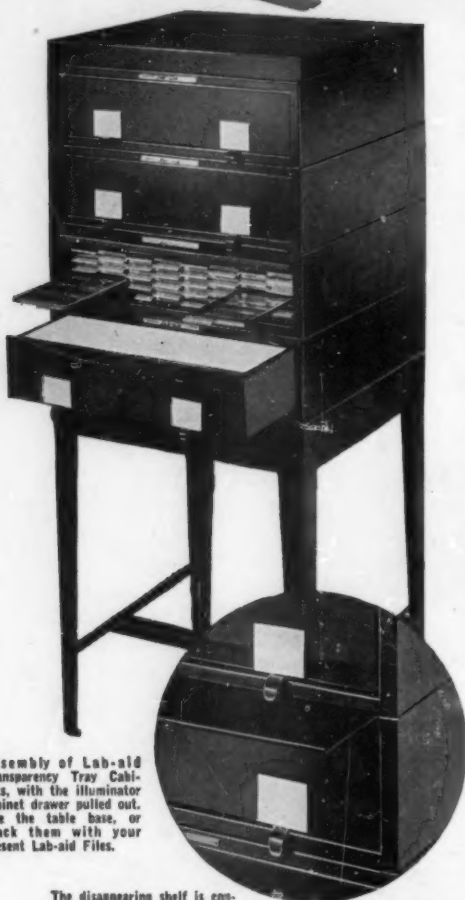
Meetings & Conferences ..... 14

Index to Volume 117 ..... i

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## Twelfth Congress of the International Association of Limnologists

**T**HE Twelfth Congress of the International Association of Limnology, of which Dr. Gunnar Alm of Sweden is president, will be held in Cambridge, England, at the Windermere Laboratory of the Freshwater Biological Association.

The Congress will open late in the afternoon of August 20 and continue through August 30. Preparations have been in the hands of the Organising Committee, with Professor F. E. Fritsch as Secretary. The scientific sessions, which will be held at Cambridge, are each divided into two or more groups, dealing respectively with the theoretical and applied sides of limnological science. To a considerable extent the papers to be read, of which approximately 100 have been offered, are grouped as symposia relating to such main topics as exchange and circulation in lakes, productivity in fresh waters, ecological and historical aspects of distribution, freshwater plankton problems, problems relating to freshwater algae, introduction of foreign species, pollution and its effects, especially in relation to fish, waterworks problems, and problems arising in connection with the treatment of sewage.

There will be two evening discourses. On August 21, Professor d'Ancona (Padua) will deliver the first Edgardo Baldi Memorial Lecture on "The Stability of Lake Planktonic Communities," and on August 25, Lt.-Col. Mackenzie, Director of Water Examinations, Metropolitan Water Board, London, will speak on

"The Reservoirs of the Metropolitan Water Board and Their Influence upon the Character of the Stored Water." On the evenings of August 22 and 24, there will be displays of relevant scientific films. On the first evening at Cambridge there will be a reception at Trinity College, and on the afternoon of August 25, a garden party at Christ's College.

The journey from Cambridge to Windermere is to be made by coach and will occupy three days (August 26-28). The theoretical and applied groups of members will follow different routes, and each will visit a number of institutions or localities of special interest on the way. At Windermere one day will be occupied by an inspection of the laboratory and a visit to the experimental hatchery and fish ponds of the Freshwater Biological Association, as well as by demonstrations of work on the lake itself, while the other will be devoted to one or another of a number of alternative tours of the Lake District. The final session of the Congress will take place on the evening of August 30.

A considerable number of excursions have been arranged. A small group of members will visit various localities of limnological interest in the south of England prior to the opening of the Congress. At Cambridge there will be excursions to Wicken Fen, the Norfolk Broads, and, for the applied section, visits to a sewage disposal works and the Water Pollution Research Laboratory. After the termination of the Congress, there will be a four-day excursion in Scotland and, subsequent to that, a week's tour in Ireland.

F. E. FRITSCH

Cambridge, England

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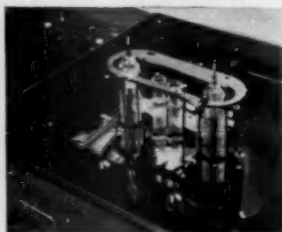
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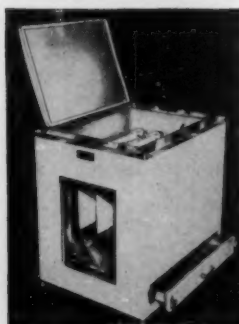
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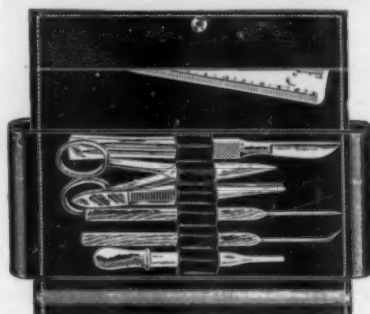
Instead he traces the evolution of scientific logic from the work scientists actually do when they inter-behave with events and construct theories and laws from their findings. Logical investigation is thus held to be continuous with original research, since the events with which the logician interbehaves are the procedures and products of scientific enterprises.

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# Does the Greater Understanding of Man and Nature Increase the Scientist's Social Responsibility?<sup>1</sup>

A. J. Carlson

*Department of Physiology, University of Chicago, Chicago, Illinois*

THE UNDERSTANDING OF MAN and of nature achieved by science is very recent. During the hundreds of thousands of years of man's past his social behavior was largely determined by direct experience, ignorance, and traditions based partly on ignorance. We have now some indications that the voluntary behavior of all sane citizens can be directed toward the best interest of mankind through the understanding and acceptance of the nature of man and the universe, as revealed by modern science. The special social responsibility of scientists is to promote this understanding on the part of all people in all nations. We must promote:

*Education through understanding versus education by dictation.*<sup>2</sup> We must have continuous adult education in all lands. Factual, that is, scientific education on the nature of man seems necessary for the best future of man. Such education includes the scientific evidence of the unity of the human race. Despite so-called racial differences in such minor details as skin color, language, and religions, science has proved that *the people now living on our earth are one species*. This fact, understood and accepted by all sane citizens, should gradually eliminate racial prejudice, fear and hate. It should promote cooperation in place of violence. Basic to the achievement of freedom from fear, want, and violence is the freedom to know.<sup>3</sup>

If the goal of education today and tomorrow is the *understanding of man and nature and action on the basis of such understanding*, it is obvious at least to me that the traditional "3 R's" and the "hundred great books" will not meet our educational needs, nor are these needs met adequately by *science alone*. But the understanding of man obviously involves man's environment and man's past, that is, history, sociology, economics, politics, literature, and even religion. The

"grass roots" as well as the "clouds" are parts of man's environments, past and present. It also means that our education is not completed at the end of the sophomore year in college or even at the end of the senior year. There must be *continued adult education* other than that provided by the modern soap operas, by propaganda, by amusement, and by artistic lying. As to so-called education or technical training, it is perfectly clear to me that we can learn by working with our hands just as well as we can by using our eyes and our ears, listening to lectures, and reading books.

I have been an investigator and a teacher of science, that is, I have tried to teach for fifty years. I think that we teachers underestimate the mental capacity of our average youths and fellow citizens. They can learn, they can understand, they can even reason, if we the teachers can really teach by word, by demonstration, by example. But we must rekindle the suppressed *natural curiosity* in our student, a curiosity largely supported by education through dictation, in the home, in the church, in the public schools, and sometimes even in our colleges and universities. Education by dictation depends on memory, faith, and tradition rather than on understanding of man and nature. The student, the teacher in every field of education should ask for the *evidence*, should examine the evidence. We cannot defeat ideas with guns or bombs or mere say so. Bad ideas can be defeated with better ideas based on better *evidence*. That is, we should apply the scientific method to our education at all levels; the scientific integrity, the scientific courage to face all the proven facts, but keep our mouths shut and our pens dry till we know the facts.

One of the difficulties in our path toward our educational goal of the *understanding of man and nature and behavior based on that understanding*, one of the obstacles, is the evident fact that the human forebrain, in which man surpasses all other species of animals, has not yet acquired complete control of the part of the brain which man has in common with the snake, the hyena, the tiger, and the goat. The second difficulty in our drive toward a better educational goal for all men in all lands is *our reluctance to think and plan for the days to come as well as for today and tomorrow*. I do not know how you stand on this issue, but to me it seems clear that we should think and act for days ahead as long as the days of our past, that is,

<sup>1</sup> Presented at the meeting of American Association for the Advancement of Science, Hotel Jefferson, St. Louis, Mo., December 30, 1952, as part of a symposium arranged by the Society for Social Responsibility in Science.

<sup>2</sup> Our British colleague A. V. Hill, said recently: "The popularizing of genuine science is an important public service; we should all be ready to take our part in it according to our powers."

<sup>3</sup> "As things now stand (science teaching in high schools and colleges) the student-citizen has a good chance of learning certain biological and physical 'facts of life' about the world in which he lives. But his chances of understanding the impact these sciences have on our society, and what he as an individual can do to control and/or modify the effects of that impact, are too often practically nil" (1).



at least a million years. It is no credit to us, it is in fact a serious reflection both on our intelligence and our integrity, to render our soil, our other resources, our social and political environment less favorable to our descendants than as inherited by our generation. It seems evident to me that a democracy cannot survive and flourish unless all citizens secure adequate understanding of man and nature through education, better factual education at all levels and throughout life; and even then we have yet to demonstrate that we are fit to survive. War in the future will come close to racial suicide.

*Cooperation versus violence and war.*<sup>4</sup> Human history, science, and reason appear to prove that it is injurious, and hence stupid, for the individual to rob, injure, or kill his fellow men. Does such behavior become beneficial to the individual and to the human race when carried out by a nation? The evidence today says no, for everybody appears to lose by violence and war. According to the German General Von Bernhardi (*Germany and the Next War*, 1911) "War is a biological necessity. War is a Universal Law of Nature." The British anthropologist, Sir Arthur Keith says (*The Place of Prejudice in Modern Civilization*, 1931): "Race prejudice, I believe, works for the ultimate good of Mankind and must be given a recognized place in all our efforts to obtain natural justice for the world. Without competition Mankind can never progress; the price of progress is competition. Nay, race-prejudice and, what is the same thing, national antagonism, have to be purchased, not with gold, but with life. Nature throughout the past has demanded that a people who seeks independence as well as peace can obtain these privileges only in one way—by being prepared to sacrifice their blood to secure them. Nature keeps her orchard healthy by pruning; war is her pruning-hook. We cannot dispense with her services." But M. F. A. Montagu (*The Nature of War and the Myth of Nature*, SCIENTIFIC MONTHLY, 1942, LIV, p. 342) speaks more wisely: "The tradition of thought which renders possible such glib talk of war and its supposed natural causes represents the bequest to us from the remote past of obsolete modes of thought which are conspicuous for their profound irrationality. So powerful is this traditional detritus that it has not failed to influence many of the most respected minds of our day, to the extent of making mathe-magicians of our mathematicians, casuists of our philosophers, and an apologist for war of the gentlest and among the wisest of our anthropologists. This tradition constitutes a Gordian knot that is so tied that to escape its bondage one must sever the knot completely—since it resists being untied. If man is to be saved from himself before it is too late this tyranny must be broken, and this can only be achieved by the unequivocal action that must follow upon the reasoned dissolution of such errors of belief and thought as

<sup>4</sup> "We may be a fixed biological species unable to change our ways, but one of the achievements of our species is that we have learned to talk things over and exchange views with one another" (2).

form so great a part of our traditional social heritage today."

*Conservation instead of waste of our natural resources.* Our future depends on our food.<sup>5</sup> Through better control of infectious diseases, more efficient repair of accidental injuries, and better knowledge of food requirements for health, modern medicine, where applied, has provided a longer and healthier life span for man. In fact, where modern preventive and curative medicine is applied and adequate food is available the human life span has more than doubled in the last 100 years. The marked decrease in infant mortality is a significant factor in the prolongation of our average life span. This influence of modern medicine can also render human life more difficult by increasing the world population beyond available food resources, thus contributing to starvation, misery, violence, and war, which are some of the consequences of starvation in all animal species.

In all species of vertebrates in the past three main factors determined the population of a species: *food supply, disease, violence, or war*. These three factors controlled also the human population practically until yesterday. By effectively diminishing disease modern medicine has significantly added to human happiness. But modern medicine also contributes to this serious world problem: *the increase of the population faster than the food production required for adequate nutrition*. What is the answer to this serious situation? Shall it be less of modern biology and medicine? more starvation? more violence and war? or more intelligence? We can, no doubt, for a while at least, get a little more food from the soil and the sea. But there is fairly good evidence that we must practically double the present world food production even to feed adequately the present world population. So far as can be judged, this cannot be done. *I think that we, in biology and medicine, must acquaint our fellow citizens with this serious world problem and aid them in working out a wise solution.*

*The survival of the most fit in our age of science.* Modern biology and medicine have not yet created sufficient factual understanding of the hereditary factors of importance in human physical and mental impairment at every age, so that intelligence rather than violence and ignorance may be applied to decrease the population increase by the significantly less fit of our species. But we know enough of some of these factors to try to establish more humane behavior than that prevailing under the biologic ignorance of the past. Life is difficult enough for people with normal physical and mental capacities. For people with less, life is largely a tragedy. And when these defects are hereditary the impaired individual is not responsible. *Again we in biology and medicine must guide our fellow citizens on this issue.*

<sup>5</sup> "If they (representatives of religions) now claim that the facts and trends of overpopulation are not what we say, we can argue about that as a scientific question: but if they insist that its consequences should be left to God, they must allow us as citizens to take the opposite view" (3).



*It seems obvious that as a citizen the scientist's social responsibility is at least as great as his understanding of man and nature. What he can contribute to a saner and happier life for man is not little, but unless we tackle this difficult task at once, it may be too late, considering current hysteria, artistic lying, fear, hate, and preparations for more destructive wars. Our age is not yet an age of science, even in our intellectually and scientifically most advanced nations. Largely through ignorance, and traditions based on ignorance as to the nature of man, we are still nourishing the malignant cancers of race prejudice, hate, fear and war. To do justice to our superior forebrain we should go forward with our eyes open. We should replace violence with intelligence. That would mean a healthier, happier future for our race. We would then be a credit to our name: *Homo Sapiens*, "Wise Men." So let us step down from our proverbial ivory tower and carry on!*

When the shadows beckon men of my years, we still have our children, we still have our dreams. I dream of a day when our leaders will actually put the principles of science and democracy to work in our land, in politics, in industry, in trade, in education; when understanding will more than hold its own against superstition, guile, and greed, when force and violence is replaced by conference, compromise, and approximate justice in all our domestic and foreign

relations. When that day is at hand in our own land, our example will be a greater impetus to the path of peace and justice in other lands, than are our present speeches, and our lend and lease of the implements of war to all democracies, and would-be democracies of the world. It is a matter of forgetting the hypothetical universe created out of ignorance and motivated by our undisciplined emotions, and a reconditioning to the actual universe as gradually understood through *controlled experience and experiment*. I think we can say, even in the face of current fears and pessimism, that during the ups and downs of the past million years man has gradually acquired more understanding, more freedom from fear, more dignity, greater kindness, and a clearer conception of justice. Even though for the moment "the bird of sorrow" is not only flying over our heads, but is actually nesting in our hair—to borrow a Chinese proverb—that bird will not nest in our hair forever, unless a blackout on science be decreed in every land. For, slowly but surely, the understanding of man provided by science will help to make our life more intelligent, toil more cheerful, fear and hatred, pain and tears less prevalent in our life.

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## Edwin Grant Conklin: 1863—1952

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WITH THE DEATH of Edwin Grant Conklin just before his eighty-ninth birthday, on November 21, 1952, there passed away one of the great interpreters of biology in the United States. Professor Conklin was born on November 24, 1863. He was a great admirer of Lincoln and proud of the fact that the year of his birth was the year the Emancipation Proclamation became effective, and proud that he had traveled in a covered wagon from one part of Ohio to another, attended a country school of one room and one teacher, and worked on a farm. Later he became the teacher in a similar country school, where he was janitor and disciplinarian as well as instructor, at a salary of \$35 a month.

One of Professor Conklin's most valuable attributes was a prodigious memory of detail, perhaps fostered by his thesis study of cell lineage. Even during the later years of his life, the date of almost any event was recalled with precision, and those of us who knew him well were entertained by many an amusing anecdote

of early life in the Middle West and of his later educational period.

After graduating from high school at Delaware, Ohio, he attended Ohio Wesleyan, obtaining a B.S. degree in 1885 and a B.A. in 1886. There he first became interested in science. This interest was fostered by trips for collecting shells and fossils under the guidance of his professor of biology and geology, Edward T. Nelson. Professor Nelson turned him toward biology, and the experience of the next three years as a teacher of Latin, Greek, and science at Rust University, a missionary college in Mississippi, matured the decision to make biology his lifework.

He entered the Johns Hopkins University Graduate School in 1888 and started work with Professor William K. Brooks. His first problem was the identification and morphology of a siphonophore collected by Alexander Agassiz in the Pacific. For continuation of these studies, he was sent to the U. S. Fish Commission Laboratory at Woods Hole, Mass. Perhaps it is fortunate that no siphonophores were obtainable there.



Turning to the varied fauna of that region, he was attracted by the abundant embryological material; and thus began the extended studies on cell lineage, first of *Crepidula*, on which he was to write his thesis, and then a similar investigation of Ascidian eggs and, later, of *Amphioxus*. In connection with the developmental history of the regions of the egg, or of the blastomeres, he studied the details of cell structure and cell division, and later performed many experiments to discover what influence environmental changes might have on the cytological picture. Embryology and cytology were his chosen fields for investigation.

Space does not permit a detailed account of the early influences in Edwin Grant Conklin's life, so important in molding his personality. Suffice it to say that the religious influence was strong in his home and in Ohio Wesleyan. Before he was seventeen, he had read the complete King James version of the Bible and committed long passages to memory. At one time he considered becoming a preacher but gave up the idea and was never ordained, although he did pass a perfunctory examination on the Bible and received what was known as a "local Preacher's license."

The ability to quote scripture served him well in later years as a popular lecturer. The controversy over evolution was at its height in the 1880's and Professor Conklin studied the subject carefully, buying personal copies of Darwin's books so that he could mark important passages for future use. The evidence convinced him completely; and the whole subject of evolution, with all its ramifications, became his life-long interest. He always spoke of evolution as "the central theme of biology, the connecting strand on which all details of the science could be strung." Later, when he accepted a teaching position at Ohio Wesleyan it was with the stipulation that he must be free to present his own beliefs regarding evolution, without censure or dictation from the university.

Evolution led naturally to a study of development. One of his favorite dicta, "Ontogeny recapitulates phylogeny," expresses this relationship well. Besides, what is more fascinating than to watch the successive divisions of the egg? I have always felt that his special interest in cell lineage was an outgrowth of the preformation-epigenesis controversy. The arguments might delight a theologian. How exciting it must have been to learn that certain cells, indeed certain regions of the egg cell itself, were always destined to become a particular part of the future organism.

Although Professor Conklin's special field of investigation was the cell, his interest in biology included the whole organism, particularly man himself. The ascidian egg and especially the embryology of *Amphioxus* may have interested him because of their status as Protochordates, ancestors of the vertebrates and thus of man.

Man's place in nature and the broader implications of biology occupied his thoughts more and more as

his career progressed. After receiving the Ph.D. degree at Johns Hopkins in 1891, he became successively professor of biology at Ohio Wesleyan (1891-1894), professor of zoology at Northwestern (1894-1896) and at the University of Pennsylvania (1896-1908), and finally departmental chairman and professor of biology at Princeton University (1908-1933). His retirement from Princeton in 1933 involved little change in activity. He took a continued interest in departmental affairs, giving seminars for graduate students in addition to writing ninety-three articles for journals, magazines, and publications of learned societies.

A broad interest in science resulted in his early election to the American Philosophical Society (1897), the National Academy of Sciences (1908), and the American Academy of Arts and Sciences (1914). The Philosophical Society "held at Philadelphia for promoting useful knowledge" particularly appealed to him because of the wide range of subjects discussed. He rarely missed a meeting, and he took a most active part in its affairs, serving on many of its committees for long periods of time, presiding at various symposia, and acting as councilor, executive officer, and vice president. He was elected president for two terms, 1942-1945 and 1948-1952.

Apart from a great loyalty to Princeton University, dating from his first years as Chairman of the Department of Biology and his association with Woodrow Wilson, then President of the University, Professor Conklin had three great outside interests to which he devoted a great deal of thought and to which his service may be said to have been really dedicated. First and foremost was the American Philosophical Society just mentioned. Another was the Marine Biological Laboratory at Woods Hole, with which he had been connected almost since its beginnings in 1888. He started teaching there in 1891 and was elected a trustee in 1897. At Woods Hole the atmosphere was and still is conducive to scientific freedom in its broadest sense: no direction of what the investigator should study, no pressure to produce premature results, only the attempt to supply the living material and the best conditions for research.

The third was the Bermuda Biological Station for Research, in which Professor Conklin had as personal an interest as its founder, Professor E. T. Mark, who was for many years its director. On reorganization of the Bermuda laboratory in 1926 Professor Conklin was made a trustee and he acted as president of the Corporation from 1926 to 1936. He was also much interested in the Academy of Natural Sciences of Philadelphia, which he served as vice president from 1901 to 1950, and in the Wistar Institute, where he had been a member of the Advisory Board since 1905 and of the Board of Managers since 1945.

Professor Conklin received many honorary degrees, was elected to membership in many foreign societies and to the editorial boards of a number of journals. At the same time his own contributions to scientific literature were voluminous. His most important book,



"a best seller," was *Heredity and Environment*, which appeared first in 1914. It passed through six editions and was translated into Japanese and Russian. Other volumes are: *Direction of Human Evolution* (1920, 1922), *Mechanism of Evolution* (1920), *General Morphology of Animals* (1927), *Problems of Development* (1929), *Freedom and Responsibility* (1935), *Science and Ethics* (1937), *Biology and Democracy* (1938), *What Is Man?* (1941), and *Man: Real and Ideal* (1943).

Throughout his life, the human interest led to acceptance of executive duties, to willingness to serve on many committees, to support various causes, all of which took time from scientific research but became the background for a far wider viewpoint than specific research could have given. He was especially interested in education and in the philosophy of religion. Commencement addresses and published pamphlets present an original viewpoint in this field. Always a liberal in outlook, he was a great believer in freedom and, like most scientists, was vehemently opposed to any sort of regulation and regimentation.

As committeeman he was a persuasive speaker, and as lecturer an eloquent one. At Ohio Wesleyan much

attention was paid to elocution and public speaking. Professor Conklin had joined a literary society, wrote poetry and essays, and took part in oratorical contests. This training and his human interest made the general biology lectures at Princeton University a popular course for many years, and he was in great demand for talks in which science is interpreted for the layman. His long association with Science Service (president, 1937-1945) and the AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (president, 1936), again reflect his broad interest in science and in man.

Professor Conklin liked nothing better than to gather around him, in the laboratory or at his home, a group of students for discussion of various subjects. These were times for reminiscence during which his listeners could learn about the history of American biology in the early part of the century from tales related with a keen sense of humor. His love of social contacts was ably supported by his wife, the former Belle Adkinson, who was always interested in his many friends and was a delightful hostess. His students and all who knew him intimately will mourn the loss of this truly great biologist and leader in science.

## News and Notes

### Federation of American Societies for Experimental Biology

THE Federation of American Societies for Experimental Biology (American Physiological Society, American Society of Biological Chemists, American Society for Pharmacology and Experimental Therapeutics, American Society for Experimental Pathology, American Institute of Nutrition, American Association of Immunology) held its thirty-seventh annual meeting in Chicago, April 6-10. The meeting was well attended, with a total registration of 6078, composed of members of the constituent Societies, visiting scientists, representatives of industries in the fields of the Federation, and guests of members. The six Societies scheduled 1389 papers at 140 scientific sessions, with an additional 153 papers read by title. Of this total, 522 were in Physiology, 454 in Biochemistry, 281 in Pharmacology, 84 in Pathology, 99 in Nutrition, and 102 in Immunology. In addition, eight symposia and panel discussion sessions were held by the Societies, and a special session presented nine motion pictures.

The Joint Session of the Federation was held on Tuesday evening, April 7, with Vincent du Vigneaud, Past President of the American Society of Biological Chemists and Chairman of the Federation Board, presiding. Three papers were presented on the general topic, "Some Aspects of Light and Biology." E. Newton Harvey of Princeton University spoke on

bioluminescence as observed in various evolutionary forms. George Wald of the Harvard Biological Laboratories discussed the mechanisms of vision. The third paper, on photosynthesis, was presented by Dean Burk of the National Cancer Institute.

Another special Federation session took place on Thursday evening, April 9, to present a report on the Survey of Physiological Science which is currently being made by the American Physiological Society, with support from the National Science Foundation. R. W. Gerard of the University of Illinois Psychiatric Institute, Chairman of the session, gave a short introductory address by way of orientation. This was followed by a progress report presented by L. M. N. Bach, Director of the Survey. Physiology in education was discussed by Orr E. Reynolds for the undergraduate and graduate schools and by J. H. Comroe for the professional schools. An evaluation of the personality patterns of experimental biologists was presented by Anne Roe, research psychologist, of New York City.

The Federation Board and the Councils of the constituent Societies met throughout the week, and Society meetings were held for the election of officers and members and the transaction of business. Dinners were scheduled for the Pharmacology, Pathology, and Nutrition Societies, and a joint smoker by the Biochemistry and Nutrition Societies was held on Wednesday evening, April 8. In addition, various other groups scheduled special meetings and dinners.



The Federation Placement Service scheduled interviews between employers and applicants and registered applicants for future openings. About 350 applicants were registered and 590 interviews scheduled by the Service at Chicago.

Exhibits by industrial firms, Society members, and institutions and laboratories were displayed in the Exhibit Hall at the Conrad Hilton Hotel, and proved to be of uniformly high quality and a most interesting feature of the convention. The fields represented included books, pharmaceuticals, apparatus and equipment, and technical demonstrations.

For the year beginning July 1, 1953, the American Society for Pharmacology and Experimental Therapeutics will be head Society of the Federation and its immediate Past President, K. K. Chen of the Lilly Research Laboratories, will be Chairman of the Federation Board; other Board members for the coming year will be: H. B. Haag and C. C. Pfeiffer, Pharmacology; C. C. Erickson and S. C. Madden, Pathology; C. A. Elvehjem, J. O. Orten, and P. L. Day, Nutrition; T. P. Magill, J. L. Sugg, and J. F. Enders, Immunology; E. F. Adolph, H. E. Essex, and E. M. Landis, Physiology; D. W. Wilson and Philip Handler, Biochemistry. M. O. Lee was reappointed Federation Secretary.

The next annual meeting of the Federation will be held in Atlantic City, New Jersey, April 10-16, 1954.

M. O. LEE

*Federation Secretary*

## Scientists in the News

Fritz G. Arndt of the University of Istanbul, Turkey, will be Visiting Professor of Chemistry at Indiana University during the first semester of the 1953-54 academic year.

George W. Beadle, Professor of Biology and Chairman of the Division of Biology at the California Institute of Technology, has been awarded the Gold Medal of the Emil Christian Hansen Foundation, Copenhagen, Denmark. The medal, which is accompanied by a prize of 5000 Danish crowns, has been awarded only 11 times since its inception in 1914. Recipients have been European and American scientists who have made significant contributions to microbiology. Professor Beadle received the award for his research in biochemical genetics using the red bread mold *Neurospora*.

Raimon L. Beard of the Connecticut Agricultural Experiment Station, formerly Executive Secretary of the Insect Control Committee of the U. S. National Research Council, has arrived in Australia to carry out research on insect diseases at the Commonwealth Scientific and Industrial Research Organization, Division of Entomology, Canberra. Under a Fulbright Fellowship, Dr. Beard will study the larvae of the cockchafer beetle, and search for bacterial dis-

eases which attack the larvae, examining the possibility of using diseases as a means of controlling these pests.

M. S. Briscoe, Assistant Professor, School of Medicine, Howard University, will collaborate this summer with the U.S. Naval Medical Research Unit No. 3 in Egypt on parasitological and entomological problems.

Carl Djerassi, Associate Professor of Chemistry at Wayne University, has been awarded an Honorary Doctor of Science degree by the University of Mexico. Until 1952, Dr. Djerassi was Associate Director of organic research at the Syntex Laboratories in Mexico City. He was one of the group of scientists who discovered the reactions making possible the first total synthesis of cortisone. The group also was able to convert materials found in the giant Mexican yam to cortisone. Dr. Djerassi has received a \$10,000 grant from the Rockefeller Foundation for research on natural plant life.

David R. Goddard, Professor of Botany at the University of Pennsylvania, has been elected Editor-in-Chief of *Plant Physiology*, the journal of the American Society of Plant Physiologists.

At McGill University, Alton Goldbloom has been named Professor Emeritus of Pediatrics and Alan Ross has been made Professor of Pediatrics. Both have received appointments at the Children's Memorial Hospital, Montreal—the first as Consulting Physician, and the second as Physician-in-Chief.

Howard B. Hutchinson, meteorologist and recently retired Captain of the U. S. Navy, has joined the Stanford Research Institute as a staff physicist. Mr. Hutchinson served from 1948 to 1952 as scientific and technical advisor to the Navy Deputy Chief of the Armed Forces Special Weapons Project of the Department of Defense, and supervised 14 field parties at the Eniwetok proving grounds.

Charles L. Leedham, Colonel, U.S. Army Medical Corps, has been appointed Chief of the Education and Training Division, Office of the Army Surgeon General, Washington, D. C. During his 24 years of military service, Colonel Leedham has held posts both in the United States and abroad, and for the past 2 years he has served as Medical Consultant for the Far East Command.

Margaret Mead, Associate Curator of Ethnology at the American Museum of Natural History, has left for the Admiralty Islands, where she will make a study of the cultural changes that have taken place during the last twenty-five years. In 1928 Dr. Mead made an intensive study of a group of children in the Admiralties; now she is returning to observe these children as adults. The first anthropologist to undertake detailed research on the children of a particular society, Dr. Mead will use new sound recording and photographic equipment in this study. The expedi-



tion is being conducted under the auspices of the American Museum with a grant from the Rockefeller Foundation.

**Emil Ott**, Director of Research for Hercules Powder Company, is in Europe as a delegate from various U.S. scientific organizations at a series of international science meetings. He is serving as an official representative at the 26th International Congress of the Société de Chimie Industrielle in Paris, the 72nd annual general meeting of the Society of Chemical Industries, and the International Congress of Pure and Applied Chemistry. He will also attend a special meeting of the UN Food and Agricultural Organization.

**Gilbert F. Otto** has resigned as Associate Professor of Parasitology at Johns Hopkins University School of Hygiene and Public Health to become head of a new Department of Parasitology in the Research Division of Abbott Laboratories at North Chicago, Ill. Dr. Otto's general field of research for the past 26 years has been worm diseases in animals and people. He has been a member of the Johns Hopkins faculty since 1927 and Director of the Parasitology Laboratory and Parasitologist to the Medical Clinics at Johns Hopkins Hospital since 1946.

**Lloyd E. Swearingen**, Director of Basic Sciences Research, and Scientific Assistant Deputy, Assistant Chief of Staff, G4, for Research and Development, Department of the Army, has been named Vice President in charge of Research and Development, University of Oklahoma.

## Education

A series of 10 short postgraduate courses will be conducted by the **Army Medical Service** during the fiscal year 1953-54. An important feature of inservice training for Medical Corps officers, these courses are also open to a certain number of civilian physicians and surgeons. Information may be obtained from the Office of the Surgeon General, Department of the Army, Personnel Division, Washington 25, D. C. Officers are requested to apply through channels.

In an unprecedented coordination of several sciences, **Columbia University** has combined the resources of three of its Faculties (Pure Science, Political Science, and Medicine) in an Institute of Human Variation, to attack some basic problems of evolution—what biological factors are responsible for variation in human beings and what are the processes by which changes occur in populations, human and otherwise. Genetics, zoology, anthropology, pediatrics, psychology, serology, and statistics contribute to the study of these problems and to the training of research experts to advance the work in this field. The three main areas of present work are the factors concerned in variations in physique, the serological and physical variations within and between groups, and

the physiological and chemical variations among human beings. **A. E. Mourant** of the Lister Institute, London, is serving the Institute as Visiting Professor of Serology. **Philip Levine**, Director of Ortho Research Foundation, is a staff member and research associate. The Director of the Institute is **L. C. Dunn**, Professor of Zoology.

Twenty undergraduate scholarships will be offered annually by the **Institute of Gas Technology**, an affiliate of Illinois Institute of Technology, to help train engineers for careers in the utility gas industry. They are available to students who have completed their sophomore year and who desire to take the gas technology option in either chemical or mechanical engineering at I.I.T. The scholarships will pay one-half of the tuition during the junior and senior years, plus \$300 for the required 12-weeks' summer term between the two years. Applications are now being accepted for the first 20 scholarships which begin in September 1953.

Faculty promotions at **Lehigh University** include: **Arthur F. Gould**, from Associate Professor to Professor of Industrial Engineering; **Douglas E. Mode**, from Associate Professor to Professor of Electrical Engineering; **Lynn S. Beedle**, from Assistant Professor to Associate Professor of Civil Engineering and Mechanics; and **Thomas S. Eichelberger**, from Instructor to Assistant Professor of Mechanical Engineering.

Approximately 120 teachers and educational administrators are registered with the **New York University School of Education** for their three overseas workshops in July and August. The seminar in England, France, and Germany will be concerned with the political and socioeconomic problems of Western Europe and the role education is playing in equipping citizens to help solve them. The second course includes a tour of Israel, designed to give a knowledge of its geography, industry, agriculture, settlements, social life, and archeological excavations. The third workshop, in Puerto Rico, will study the life and customs of the island and the problems of adaptation and adjustment of its children who come to the mainland. The New York City teachers participating in the Puerto Rico workshop are winners of maintenance scholarships provided by the Puerto Rican government in cooperation with NYU and the University of Puerto Rico.

Seven members of the scientific faculty at **Stevens Institute of Technology** have been promoted. Advanced from Associate Professor to Professor were **Arthur Lesser, Jr.**, who becomes **Alexander Crombie Humphreys** Professor of Industrial Engineering, and **Carl Neitzert**, Professor of Electrical Engineering. Promoted from Assistant to Associate Professor were **Adam Abruzzi**, Industrial Engineering; **Reuben Benumof**, Physics; and **Edward Peskin**, Electrical Engineering. **James J. Lawlor**, Machine Design, and



John E. Nankivell, Physics, formerly Instructors, were named Assistant Professors.

Three new appointments have been made to the University of Illinois faculty. Sam S. Barkulis of Western Reserve University has been named Assistant Professor of Biological Chemistry in the College of Medicine. Joseph Larner of Washington University School of Medicine has been named Assistant Professor of Biochemistry. Norman F. Oebker of Cornell University was named Assistant Professor of Horticulture.

## Grants and Fellowships

Fourteen unclassified physical research contracts with universities and private research institutions, awarded by the U.S. Atomic Energy Commission, are part of the AEC's continuing policy of assisting and fostering private research and development to encourage maximum scientific progress in fields related to atomic energy. All contracts are for basic research.

The institutions under contract, the titles of the research, the individuals who will conduct the research, and the amounts awarded are listed below.

*Brown University*, Precision Measurements of Neutron Interactions, R. A. Peck, Jr., \$17,469; *University of California*, Research on Fluorocarbons Solutions, R. L. Scott, \$10,435; *University of Chicago*, Research on the Structure and Properties of Graphite, L. Meyer, \$13,471; *Columbia University*, Ion Exchange Chromatography, W. A. Selke, \$2,474; *University of Connecticut*, Inelastic Scattering of Neutrons, S. S. Friedland, \$36,422; *Florida State University*, Search for Long-Lived Radioactivities and Including Theoretical Nuclear Studies, R. K. Sheline, \$10,442; *George Washington University*, Studies of Fluorides of the Rare Earth Elements, C. R. Naeher, \$5,115; *Indiana University Foundation*, Electrochemical Research in Aqueous Solutions, W. B. Schaap, F. C. Schmidt, \$13,290; *Ohio State University Research Foundation*, Modification of the 42" Cyclotron, H. Hausman, \$2,600; *Pennsylvania State College*, Neutron Single Crystal Structure Analysis, R. Pepinsky, \$8,829; *Purdue Research Foundation*, Studies in Molecular Spectroscopy, W. F. Edgell, \$29,800; *University of South Carolina*, Use of Carbon-14 in a Study of Alkyl Fluorination, H. W. Davis, \$1,776; *Western Reserve University*, Thermodynamic Properties of Gases Adsorbed on Solids, E. L. Pace, \$10,780; *Yale University*, High Energy Physics, H. L. Kraybill, E. C. Fowler, \$30,348.

The Committee on Growth of the National Research Council, acting for the American Cancer Society, is accepting applications for grants-in-aid in support of cancer research. Applications for new grants received before Oct. 1 will be considered during the winter and grants recommended at that time will become effective July 1, 1954.

The Committee feels that a clear understanding of cancer must rest upon a deeper insight into the nature of the growth process, normal and malignant. Therefore, the scope of the research program is very broad and includes, in addition to clinical investigations on cancer, fundamental studies in the fields of cellular physiology, morphogenesis, genetics, virology, biochemistry, metabolism, nutrition, cytochemistry, physics, radiobiology, chemotherapy, endocrinology and environmental cancer.

During the past year the Society, on recommendation of the Committee on Growth, has awarded approximately 250 grants totaling more than \$1,700,000.

A program of similar magnitude is contemplated for the coming year. Additional information may be obtained from the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Ave., Washington, D. C.

The Travel Committee of the Genetics Society of America has raised a sum of money to assist members to attend the 9th International Congress of Genetics which will be held in Bellagio, Italy, Aug. 24-31, 1953. Contributing organizations include: National Science Foundation; American Cancer Society; Damon Runyon Memorial Fund for Cancer Research; Rapkine French Scientist Fund; Kimber Farms, Niles, Calif.; Nicholas Poultry Farm, Kingston, N. H.; Carworth Farms, New City, N. Y.; DeKalb Agricultural Assoc., Ill.; Ferry Morse Seed Co., Detroit; Associated Seed Growers, New Haven; Dover Publications, New York; W. H. Freeman & Co., Publishers, San Francisco; New American Library of World Literature, New York; Eli Lilly & Co., Pharmaceuticals, Indianapolis.

Each of the following 37 members of the Society has been granted a travel award of \$300, according to W. R. Singleton, Chairman of the Award Committee: NSF Grants—David Bonner, Meta Brown, Hampton L. Carson, Ernst Caspari, Ruth V. Dippell, Allen S. Fox, Joseph C. Gall, Eldon Gardner, Melvin Green, R. P. Levine, C. P. Oliver, A. H. Sparrow, Kathryn F. Stein, Mildred Swann, and Bruce Wallace. Other Funds—Vernon Bryson, W. J. Burdette, C. R. Burnham, J. W. Cameron, Herman Chase, Norman Giles, H. B. Glass, Aloha Hannah, William Hovanitz, Walter Landauer, Harlan Lewis, J. B. Lush, Helen U. Meyer, Herschel Mitchell, Mary Mitchell, F. J. Ryan, George Snell, Tracy Sonneborn, Clyde Stormont, Herluf Strandakov, I. Juan Valencia, and Henry Vogel.

In addition, more than one hundred other American geneticists have expressed their intentions of attending the Congress. One group of more than 20 will sail on the *M/V Georgic* on July 22. The President of the Congress will be Professor Richard Goldschmidt of the University of California, who receives \$500.

Five Merck Senior Postdoctoral Fellowships in the Natural Sciences have been awarded through the National Research Council. The fellowships are granted for the purpose of giving advanced education and training to young scientists in physics, chemistry, or biology, who wish to broaden their fields by acquiring familiarity with other areas. The five fellows and the institutions at which they will study are: Paul J. Allen, University of Sheffield; Donald H. Bucklin, Harvard University; Edwin W. Fager, Oxford University; Morgan Harris, Université de Paris; and Robert G. Parrish, Cambridge University.

Twelve Postdoctoral Fellowships in the Natural Sciences have been awarded for 1953-54 by the National Research Council, supported by the Rockefeller Foundation. Winners and the institutions at



which they will study are: Paul W. Berg, Stanford; Stephan A. Berko, Princeton; Joseph B. Griffling, University of Cambridge; Donald G. Higman, McGill; Lionel F. Jaffe, Hopkins Marine Station; Rolf W. Juhle, University of California at Berkeley; Arthur K. Kerman, California Institute of Technology; Frederiek M. Richards, Carlsberg Laboratorium; Zevi W. Salsburg, University of Amsterdam; Edgar W. Warnoff, Birkbeck College, University of London; Joe L. White, Rothamsted Experimental Station, Harpenden, England; and William N. White, California Institute of Technology.

## Meetings and Elections

The American Fern Society announces the following program of meetings and field trips to be held during the next three months. These meetings are open to anyone interested in the study of ferns. Bulletins are now available for the two longer field tours for which registration should be made at least three weeks in advance.

July 18. New Canaan Bird Protective Society, New Canaan, Conn. For information address Miss Alice Bristow, Silvermine Road, Norwalk, Conn.

Aug. 14-19. In New York State: Pilot Knob, Lake George, Wilton, Paradox Lake, Ausable Chasm, Lake Champlain; In Canada: St. John and Montreal. For information address R. C. Benedict, Pilot Knob, N. Y.

Aug. 30-Sept. 5. Central and Northern Michigan. For information address Mrs. Kathryn E. Boydston, Niles, Mich. Sept. 7-8. Madison, Wis. In association with the American Institute of Biological Sciences, papers and one-day field trip. For information address Dr. Herbert Clarke, University of Wisconsin, Madison.

The Society for Investigative Dermatology has elected the following officers for the year 1953-54: president, Arthur C. Curtis, University Hospital, Ann Arbor, Mich.; vice president, Francis W. Lynch, 1466 Lowry Medical Arts Bldg., St. Paul, Minn. Herman Beerman was reappointed designate of the Society to the AAAS. The 1954 meeting will be held June 19-20, 1954, at the Clift Hotel, San Francisco.

The Society of Rheology will hold its annual meeting at the Hotel New Yorker, October 29-30, 1953. The Program Committee invites contributions from members of the Society and from others who are interested in rheology. Papers on fundamental studies of flow, plasticity, elasticity, and viscoelastic phenomena are among those which are appropriate, as are contributions dealing with practical applications of rheology, and those describing pertinent instrumentation. Correspondence concerning papers should be sent to John H. Elliott, Chairman, Program Committee, Hercules Experiment Station, Wilmington, Delaware.

A 10-nation conference of fisheries and oceanographic experts was held in May at Yale University. A. Vedel Taning of the Danish Institute for Fishery Investigations, G. Rollefson of the Institute for Marine Research at Bergen, Norway, and Herbert W. Graham and Clyde C. Taylor of the U. S. Fish and Wildlife

Service read papers pooling evidence that the North Atlantic is in the midst of its warmest period in hundreds of years. Definite steps were taken to set up a research program into Atlantic atmospheric and temperature conditions for the future. The Conference chose Halifax, Nova Scotia, as the site of its permanent headquarters.

## Miscellaneous

Two \$1000 AAAS-George Westinghouse Science Writing Awards will be made for the outstanding science stories of the 1952 contest year. Awards are made in two classes—magazine and newspaper science writing. Financed by a grant from the Westinghouse Educational Foundation, the awards will be presented at the AAAS meeting in Boston. Magazine entries must have appeared in nontechnical publications widely read by the lay public, and in both competitions only entries that have been published between Oct. 1, 1952, and Sept. 30, 1953, will be considered. Newspaper writers must submit two separate science stories in addition to the one they designate as their entry. Inquiries should be addressed to AAAS-George Westinghouse Science Writing Awards, 1515 Massachusetts Ave., N.W., Washington 5, D. C.

Recent foreign visitors at U. S. government agencies included: at the Bureau of Agricultural and Industrial Chemistry's Eastern Regional Research Laboratory, Philadelphia; Nobuyo Shigemastu, Tokyo; Walther Fachmann, Duisdorf; S. W. Souci, Munich; H. Phillips, Surrey, Eng.; and P. Chambard, Lyon, France; at the National Bureau of Standards: S. D. Sinval, Lucknow; Evert Jan Post, The Hague; H. T. Mitchell, London; Marwan Nasr, Beirut; Peter A. King, Manchester; R. de Strycker, Louvain; Koji Ohya, Shuichi Kan, and Akira Aoki, Osaka; Koichiro Obama, Kawasaki; Gustavo Jacobsthal, Guatemala; Holde B. Levi, Copenhagen; C. B. Venton, Queensland; Frank Gill, London; and H. G. Kuessner, Göttingen.

The National Geographic Society has completed the largest map-making project in the 55-year history of its cartographic section, as a result of which a new 10-color historical map of the United States is being distributed. The map is 41 x 26½ inches in size, and is being distributed with the June issue of the *National Geographic Magazine*.

The following rare chemicals are wanted by Armour Research Foundation of Illinois Institute of Technology, Registry of Rare Chemicals, 35 West 33rd Street, Chicago: Ruthenium nitrate; Niobium nitrate; Di-tert-butyl magnesium; 2,4'-Diphenic acid; Hydrazine nitrate; 2,4,4-Trimethylpentanone-3; 4-Chloroproline; 3-Amino-2-naphthoic acid; 3-Nitro-2,5-dichlorothiophene; 8-Octadecene; Tetramethylethylene oxide; 2-Methyl-5-vinylpyridine; 2-Methylpentanal; 1,7-Dimethylxanthine; Peroxidase; Sphingosine sulfate; Pyocyanine; Urobilin; Zymosterol.



# Technical Papers

## Propagation of Group A Cocksackie Viruses in Denervated Adult Mouse Muscle

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National Institutes of Health, Bethesda, Maryland

Evidence in the literature (1, 2) indicates that denervation of adult skeletal muscle results in decrease in activity of two enzymes: phosphorylase and phosphoglucosylase, toward the low levels found in embryonic and infant muscle. The concept that denervated muscle may resemble immature muscle in some aspects of its metabolism suggested that the metabolic change in denervated muscle might result in a return to the ability of the tissue to support the multiplication of the Group A Cocksackie viruses. These viruses previously have not been demonstrated to undergo multiplication in adult mice; Syverton *et al.* (3) have reported that following the simultaneous administration of cortisone and x-irradiation, a Group A, Type 4, Cocksackie virus was lethal for adult mice; however, no evidence was presented to prove that viral multiplication had occurred or to indicate that muscle was affected.

Five- to six-week-old white Swiss mice were subjected to unilateral sciatic nerve section in the thigh, and approximately 2 weeks later were inoculated intramuscularly into the calf of the denervated leg with a dilution of a Group A, Type 2, Cocksackie virus (N.I.H. strain 93). Three days after inoculation the gastrocnemius muscle was removed and the infectivity titer determined in 2-day-old mice. It has been found repeatedly that following inoculation of  $10^3$ – $10^4$  LD<sub>50</sub> (determined in 2-day-old mice) the infectivity titer of the muscle reached  $10^5$ – $10^6$ . In controls, consisting of normal adult mice, or of adult animals subjected to a sham operation, only traces or no virus remained on the third day. Strain 93 has been carried without difficulty through 50 serial passages in denervated adult mouse muscle, each passage being made by the injection of 0.02 ml of a 2.5% muscle suspension into the denervated calf. The infectivity titer of the 50th passage muscle was  $10^{6.1}$ . Material from the 50th adult passage was typed serologically as strain 93.

For initiation of infection by the intramuscular route, an interval of at least 7 days after denervation and an inoculum of at least 3 logs of virus (LD<sub>50</sub>'s in suckling mice) are required. Preliminary experiments indicate that the infection is confined to the denervated limb. Infection of the denervated muscle is occasionally initiated when large doses of virus are given intraperitoneally, but not when given orally.

Strains representing 7 additional types of Group A

Cocksackie viruses have been tested, and evidence of multiplication has been obtained in all; no conclusive evidence of growth in controls has been found, and attempts to pass the viruses serially in sham-operated mice have been consistently negative. Two strains, representing Albany Type 3 and Type H<sub>3</sub>, have been carried successfully through 7 serial passages in denervated adult mouse muscle, with virus present at theoretical dilutions of the original inoculum of  $10^{-23}$ .

Although the hypothesis of the reversion of the muscle metabolism to that of immature muscle is attractive in regard to the ability of the denervated muscle to support the growth of the Group A Cocksackie viruses, the available data are not sufficient to warrant any conclusions on the mechanism of the phenomenon.

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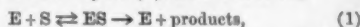
Manuscript received November 21, 1952.

## Catalase Assay with Special Reference to Manometric Methods<sup>1</sup>

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The Michaelis-Menten concept of the mechanism of enzyme action has been very fruitful in correlating the rate of a catalyzed reaction with the concentration or "activity" of the enzyme (1). In the reaction



where E is the free enzyme and S the substrate, the rate of breakdown of the intermediate complex, ES, is assumed to be rate-determining. Since in the presence of excess substrate all the enzyme is in the form of ES, the monomolecular breakdown of ES is linearly proportional to the total enzyme concentration. The concentration of the intermediate complex under these conditions is constant, and therefore the rate of the reaction obeys a zero order equation with respect to substrate concentration. These properties of a Michaelis-Menten type of enzyme provide the basis for the rationale for computing enzyme concentrations from a zero order slope.

The same rationale cannot be used for catalase,

<sup>1</sup> This work was done under an American Cancer Society Fellowship recommended by the Committee on Growth of the National Research Council.

<sup>2</sup> Present address: Division of Physical Biochemistry, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland.



however. The substrate species reacts twice with the enzyme, first with the free form, then with the primary complex (3-4):



The second step, a bimolecular reaction, is only partially rate-determining. Moreover, the kinetics of the destruction of hydrogen peroxide by an uninhibited catalase is well established as a readily integrable first order process with respect to the substrate concentration (5, 6):

$$ds/dt = -k_0(s), \quad (4)$$

where  $k_0$  is the observed first order velocity constant (with the dimensions of  $\text{sec}^{-1}$ ) for a given concentration of enzyme, and  $(s)$  is the substrate concentration. The value of  $k_0$  is independent of substrate concentration ( $10^{-5}$  to  $10^{-1}$  M) or time and is found to be linearly proportional to the enzyme concentration. Equation (4) may be written thus:

$$ds/dt = -k_s(e)(s), \quad (5)$$

where  $k_s$  is the specific reaction rate (with the dimensions of  $\text{liter} \times \text{mole}^{-1} \times \text{sec}^{-1}$ ) and  $(e)$  is the enzyme concentration. Since the molar concentration of the catalase can be determined spectrophotometrically (6),  $k_s$  can be readily calculated from Eqs. (4) and (5):

$$k_s = k_0/e. \quad (6)$$

Conversely, once  $k_s$  is known, Eq. (6) may be used to calculate  $(e)$  from the observed values of  $k_0$ . Equation (6) is valid for rates calculated from measurements of either the destruction of hydrogen peroxide or the oxygen evolution.

Despite the fact that these relations have been known for several years (6), the majority of papers published on catalase since 1947 (7-13) (with the exception of the series by Chance [4] and others [2, 6, 14]), have presented calculations of the concentration, degree of inhibition, or thermodynamic properties of catalase by means of "activity" measurements which bore no linear relation to the mass action laws governing the catalase-hydrogen peroxide reaction. For this reason, the data cannot be quantitatively compared nor the conclusions considered unequivocal. Quantitative methods for studying the rate of peroxide breakdown by catalase as a function of catalase concentration must yield data that meet the following criteria:

(a) The concentration of the active enzyme always must be linearly proportional only to a first order velocity constant (which does not contain the substrate or product concentration as a dimension), and (b) the first order velocity constant must be independent of substrate (or product) concentration and time. It follows that any velocity constant to be substituted in any of the thermodynamic equations must be calculated from Eq. (6).

For illustrative purposes and because of its extensive use, the manometric method of assaying catalase "activity" will be considered. The special problem of

oxygen diffusion across the air-liquid interface makes the analysis of kinetics by the manometric method difficult. Precautions have been taken by several authors to compensate for this difficulty (10, 15), but in none of the experiments did the observed rate of oxygen evolution follow a strict first order equation. The initial lag in oxygen evolution commonly observed (11, 16) has no theoretical basis in the catalytic process (2). Reasons for the failures of these methods are discussed by Lewis and Whitman (17), Adney and Becker (18), and Roughton (19), where diffusion of insoluble gases across air-liquid interfaces is considered.

The usual manometric technique was employed in two studies (16, 20). The rate of evolution of oxygen from 2.5 ml of reaction mixture containing beef liver catalase (Worthington), varying concentrations of hydrogen peroxide (0.037-0.20 M) dissolved in 0.05 M borate buffer, pH 7.8, was followed in a Warburg-Barcroft manometer at 5° C. Figure 1 shows curves of oxygen evolution at three different rates of agitation at constant enzyme and initial substrate concentrations. Both the rate and the order of the rate of oxygen evolution increased with increasing rates of

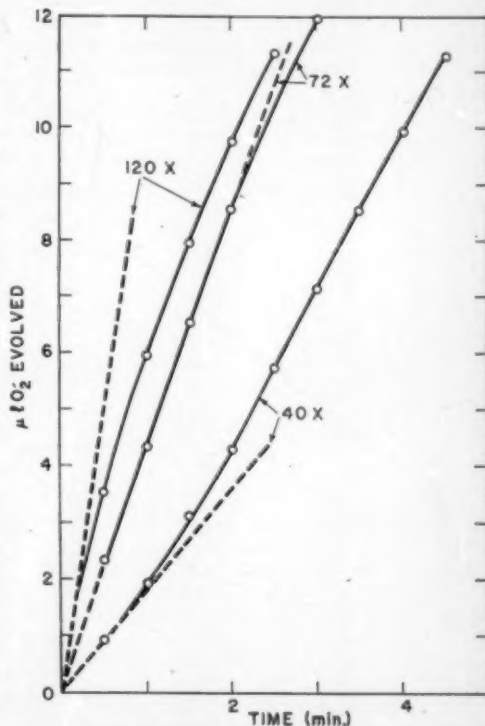


FIG. 1. Effect of varying rate of oscillation of Warburg cups from 40 to 120 times/min. Dashed lines are extrapolated initial rates. Stock solution of catalase diluted 1:200,000. Initial hydrogen peroxide concentration 0.073 M.



agitation. The initial lag, as expected, is most apparent at the lowest rate of agitation. This lag can be abolished by increasing the substrate concentration. Figure 2 illustrates the illusion of saturation of the enzyme by increasing the substrate concentration. Beyond a given concentration of substrate at a given rate of agitation, increasing the substrate concentration has no apparent effect on the rate of evolution of oxygen. The fallacy of the hypothesis of enzyme saturation is further supported by the additional finding that increasing the enzyme concentration under these same conditions increases the oxygen evolution at a rate almost linearly proportional to the enzyme concentration except at low enzyme concentrations (Fig. 3). In addition, the apparent saturation value of the substrate concentration increases with enzyme concentration. However, as the rate of agitation increases, the so-called "saturation value" of the substrate increases (Fig. 2). Control studies using titrimetric methods (15, 20) show that the agitation rate itself has no effect on the catalytic process. Therefore, the above phenomena are artifacts of the manometric method and are due to the peculiar compensatory action of the first order catalytic process and the limiting rate of transfer of oxygen across the air-liquid interface. Since the criteria for studying catalase kinetics have not been met, this particular manometric method must be considered unsatisfactory for catalase assay.

It is hoped that with an increased awareness of the kinetic properties of the catalase-hydrogen peroxide system, future investigators will employ methods that

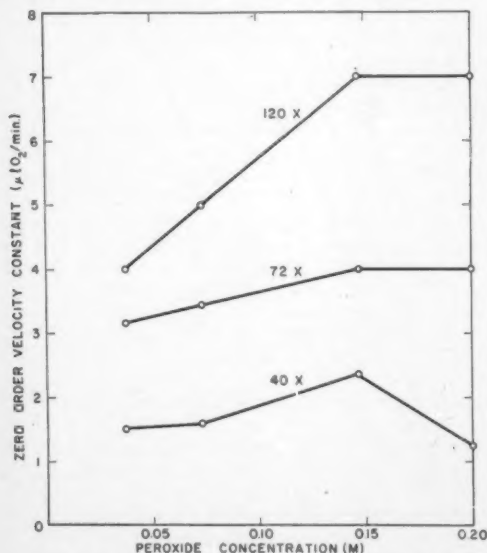


FIG. 2. Effect of varying substrate concentration and rate of agitation on rate of evolution of oxygen. Linear portion of slope used for rate calculation. Catalase stock solution diluted 1:250,000.

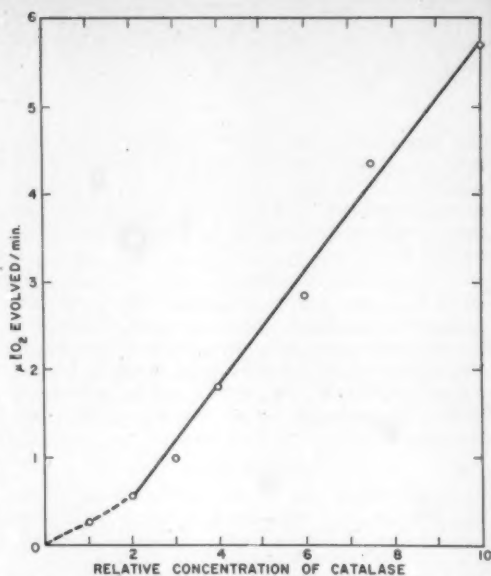


FIG. 3. Apparent linearity between rate of oxygen evolution and enzyme concentration. Rate of agitation 120 times/min. Initial peroxide concentration 0.073 M. Catalase diluted 1:125,000 to 1:12,500. See text for details.

record the true rate of the reaction (or some linear function thereof) and will use rate constants consistent with the mass action laws. It is apparent from this study that, because the kinetics of the catalase-peroxide system are known, it becomes possible to specify rigorous criteria for quantitative assay methodology which permits adequate calculations of rate constants.

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# A Quantitative Amino Acid Analysis of Sheep Adrenocorticotropic (ACTH) Protein<sup>1</sup>

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The amino acid analysis of sheep adrenocorticotropic (ACTH) protein, prepared by the method of Li, Evans, and Simpson (1) is presented. Three investigators working independently and in separate laboratories have produced these results. The starting material in each case was taken originally from the same bottle, thus eliminating any question as to differences in results being caused by variations in preparative technique. The analyses may, therefore, be directly compared.

passage through the column. Thus, known quantities (1.2  $\mu$ M) of each amino acid were added to the column and the total optical density of the developed ninhydrin color was recorded for each peak, being determined with the Beckman DU spectrophotometer. The standardization was performed 3 or 4 times for each amino acid and the average value used in the determination of the unknown. In so doing, the ratio of optical densities of unknown to standard multiplied by 1.2 equaled the number of micromoles of the particular amino acid under consideration in a known quantity of the chromatographed protein hydrolysate.

Table 1, method 1, presents the data obtained by Shankman Laboratories (6, 7) using microbiological techniques, except for cystine which was determined by Li (8). Methods 2 and 3 present the data obtained by Hier (9), using microbiological techniques, and those of the author, respectively.

TABLE 1  
AMINO ACID ANALYSIS OF ADRENOCORTICOTROPIC (ACTH) PROTEIN

Amino acid	Amino acid content of protein (g/100 g)				Estimated number of residues			
	Method*	1	2	3	Av	1	2	3
Alanine	—	—	—	7.04	7.04	—	—	18
Arginine	8.7	9.0	—	10.28	9.3	11	12	13
Aspartic acid	6.7	6.3	—	6.83	6.6	11	12	12
Cystine	7.2	8.6	—	8.21	8.0	7	8	8
Glutamic acid	15.6	16.1	—	14.99	15.6	24	25	23
Glycine	8.0	—	—	8.66	8.3	24	—	26
Histidine	1.3	1.3	—	1.34	1.3	2	2	2
Isoleucine	3.1	3.4	—	2.97	3.2	5	6	5
Leucine	7.8	7.2	—	7.42	7.5	13	12	13
Lysine	5.0	4.6	—	5.32	5.0	8	7	8
Methionine	1.9	1.2	—	0.91	1.5†	3	2	—
Phenylalanine	4.0	4.2	—	4.13	4.1	5	6	6
Proline	8.2	7.7	—	9.61	8.5	16	15	19
Serine	6.0	—	—	6.69	6.2	13	—	14
Threonine	3.2	2.1	—	3.63	3.0	6	4	7
Tyrosine	2.4	2.4	—	2.99	2.6	3	3	4
Valine	3.4	3.3	—	3.49	3.4	7	6	7
Method					Mean Molecular Weight ± Standard Deviation			
1					22,600			
2					22,900			
3					22,900			

\* See text.

† Chromatographic value not included in the average.

The method used by the author was essentially the starch-column chromatographic technique of Moore and Stein (2-5). The only major departure from their procedure was the standardization of the amino acids. Although they used color recovery, the method used in these determinations was based on amount of color developed from the eluted amino acid without concern for that which might be lost in some manner during

Three sets of data are included in the table for comparative purposes. The calculated molecular weights of the protein by the 3 analyses are not significantly different, nor is the spread of the 3 sets of values significantly different. For the molecular weight estimation from the chromatographic data, the value for methionine was omitted, apparently being too low. The sum, however, of the methionine plus cystine sulfur is 2.38%, while the data from method 1 yields a sum of 2.33%.

The chromatographic values for serine and threonine are corrected according to Rees (10). If these correction factors for loss during hydrolysis are ne-

<sup>1</sup> This work was supported in part by grants from the U. S. Public Health Service, the Armour Laboratories, and the Merck Co., and was taken, in part, from a section of the author's thesis submitted in partial satisfaction of the requirements for the Ph.D. degree in Biochemistry at the University of California, Berkeley.

<sup>2</sup> Cutter Laboratories Fellow in Biochemistry, 1950-51.



glected, the values become 5.96 for serine and 3.41 for threonine as g per 100 g protein.

The estimated number of amino acid residues per molecule of protein appears in the second set of figures for each method. A comparison of these numbers reveals the 3 determinations to agree on histidine only; although aspartic acid, cystine, isoleucine, leucine, lysine, phenylalanine, tyrosine, and valine show agreement in 2 out of 3 of the analyses. In the latter 8 instances, 7 of the identical sets of numbers include the chromatographic data, whereas one set includes the 2 microbiological data. If the uncorrected chromatographic data for serine were used, it would agree with one of the microbiological figures for this amino acid. The remaining numbers do not show agreement although the differences are not large, except for the chromatographic values for methionine and proline.

The preponderance of acidic over basic amino acids is in keeping with the isoelectric point of the protein (11) and also points to a site of action for the cationic exchange properties which this protein quite possibly displays (12).

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### $P^{32}$ Distribution in the Serum Proteins of the Chicken<sup>1</sup>

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The source of the phosphorus found in the egg has been the subject of numerous investigations and, in general, these studies have shown that extra phosphorus appears in the blood of birds during egg formation. In this respect, the relationship between the phospholipids and the site and rate of formation of these substances has been discussed previously (1, 2). Recently, differences in the number and amount of the electrophoretic components of the serum proteins of laying and nonlaying birds have been observed (3, 4); however, except for the possible lipoprotein nature of certain of these components (4), no other characteristics have been reported. According to Chargaff (5), phosphorus plays an important role in binding the lipid to the protein, and the amount of phos-

phorus found in various lipoproteins tends to confirm this statement. A method for measuring the  $P^{32}$  distribution in the various components of protein mixtures is now available (6), and by using this technique the  $P^{32}$  in the electrophoretic components of the sera of birds has been under investigation. Certain of the results, and the relationship of these results to the distribution of the lipoprotein fractions reported by Moore (4), are discussed in this communication.

The sera were prepared from the blood of 8-week-old chickens, from 8-week-old chickens injected with diethylstilbestrol, and from laying hens. The 8-week-

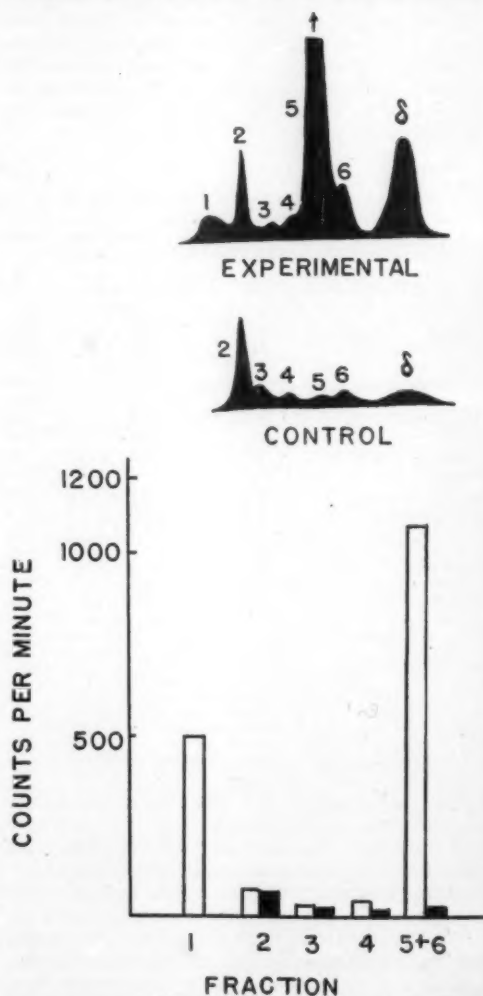


FIG. 1.  $P^{32}$  activity of the electrophoretic components of the blood serums of normal and diethylstilbestrol-treated chickens. The solid bars represent the activity of the components of the control; the open bars represent the activity of the hormone-treated birds.

<sup>1</sup> Contribution No. 480, Department of Chemistry.



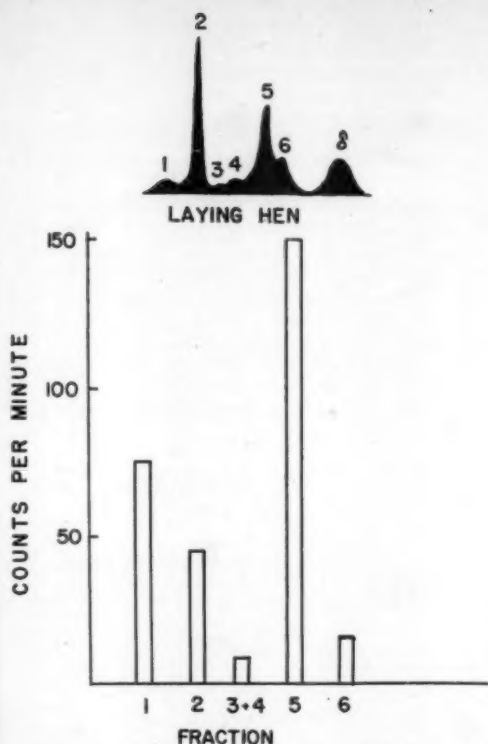


FIG. 2.  $P^{32}$  activity of the electrophoretic components of the blood serum of laying hens.

old chickens were fed 1 mc of  $P^{32}$  daily for 3 or 4 days, and the laying hens were fed in a similar fashion for 7 days. The electrophoretic (3) and radiochemical (6) techniques have been described elsewhere. For the purpose of this discussion the plateaus of the  $P^{32}$  activity curve have been subtracted one from the other so that the activities shown in Figs. 1 and 2 represent the relative activities of the various electrophoretic components.

The chief difference in the radioactivity associated with the sera of the normal nonlaying birds and those injected with the diethylstilbestrol was the high  $P^{32}$  content of 2 of the electrophoretic components. As illustrated in Fig. 1, component 1 and the greatly enlarged component 5, which are present only in the hormone-treated birds, contained relatively high concentrations of  $P^{32}$ . In the case of the laying hens (Fig. 2), the same phenomena were evident. The lower total amount of activity in the laying hens was probably caused by the loss of  $P^{32}$  in the eggs during the experimental period, however, inasmuch as the same pattern was present in both the laying and hormone-treated birds.

Moore (4) has shown that the ether extraction method of McFarlane removed the extra or enlarged

components found in the sera of laying and hormone-treated birds. The fact that repeated freezing at  $-25^{\circ}\text{C}$  and thawing was needed to remove the fat-soluble substances is indicative of the presence of rather stable phospho-lipo-protein complexes and demonstrates the absence of mixtures or loosely adsorbed systems. With this in mind the fractionation and properties of these components are under investigation.

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#### Degradation of Glucose<sup>1</sup>

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The original method of glucose degradation (1), based on bacterial conversion of glucose to lactic acid and subsequent chemical degradation, was laborious and time-consuming. Aronoff and Vernon (2) suggested a chemical method that appeared more satisfactory. Glucose was converted to its osazone which was then oxidized by periodic acid. The products of oxidation were: formaldehyde from C-6, formic acid from C-4 and C-5, and the osazone of mesoxalaldehyde from C-1 + C-2 + C-3. Further oxidation of the osazone of mesoxalaldehyde with 1% alcoholic potassium hydroxide should yield glyoxalosazone derived from C-1 + C-2. However, Vittorio, Krotkov, and Reed (3) reported difficulty in isolating glyoxalosazone from this oxidation and were forced to adopt a modified technique involving precipitation of acetaldehyde as aldolmedone.

Osazones are unstable compounds and have generally been discarded in favor of the phenylosotriazoles as characteristic derivatives of sugars. It was, therefore, decided to try the Aronoff and Vernon procedure, with slight modifications, on the stable phenylosotriazole derivative of glucose. The scheme of this degradation is shown in Fig. 1.

Glucose (I) was converted to glucosazone (II) (4) which was changed to glucose phenylosotriazole (III) (m.p.  $194-195.5^{\circ}\text{C}$ ,  $[\alpha]_{\text{D}}^{25} = 79.3$ ,  $C = 1.01$  in pyridine) by the method of Hann and Hudson (5). Periodate oxidation of III, as reported by the same authors (5), yielded 1 mole of formaldehyde from C-6, 2 moles of formic acid from C-4 and C-5, and 2-phenyl-4-formyl osotriazole (IV) from C-1 + C-2 + C-3. Com-

<sup>1</sup> N.R.C. No. 3014.

<sup>2</sup> The author wishes to thank G. A. Adams for calling attention to this problem. The technical assistance of J. E. Fraser is gratefully acknowledged.



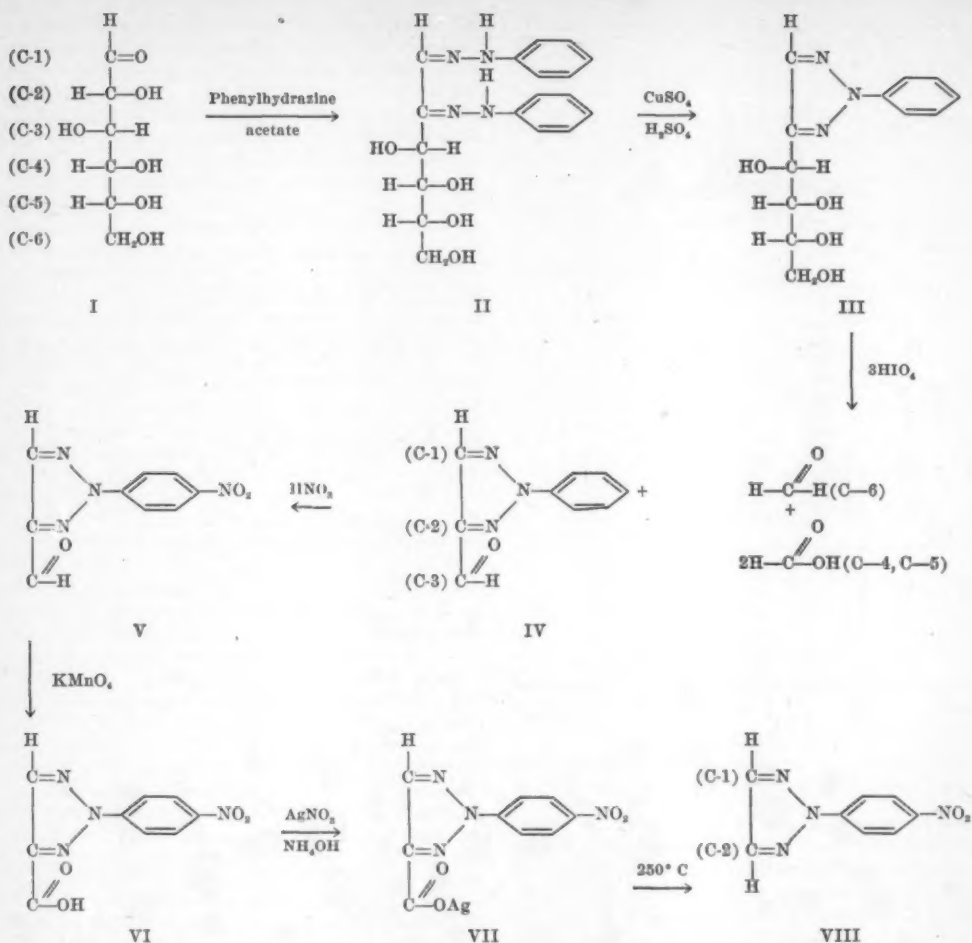


FIG. 1. Scheme for glucose degradation.

compound IV was filtered from the periodate oxidation as colorless crystals having the reported m.p.  $69-70^\circ\text{C}$  (5, 6). Nitration of IV with fuming nitric acid at room temperature (6) yielded 2-(p-nitrophenyl)-4-formyl osotriazole (V), m.p.  $136-137^\circ\text{C}$ , reported here for the first time. Infrared absorption spectra supported the proposed structure and the results of analysis agreed with the calculated values.

Calculated for  $\text{C}_9\text{H}_8\text{O}_5\text{N}_4$ : C = 49.54%, H = 2.77%, N = 25.68%. Found: C = 49.41%, H = 3.03%, N = 25.51%. Further confirmation of the structure of V was given by the next step in the degradation: Alkaline permanganate oxidation (7) produced the acid, 2-(p-nitrophenyl)-4-carboxy osotriazole (VI) which was recrystallized from water to a constant m.p.  $236-237^\circ\text{C}$ , in agreement with the reported value (6). The

silver salt of VI was formed by heating the acid in ammoniacal silver nitrate until solution was complete. Three volumes of a mixture of acetone : methanol (1 : 1 by volume) were added and the solution was boiled gently to remove ammonia. The removal of ammonia caused the precipitation of the silver salt of 2-(p-nitrophenyl)-4-carboxy osotriazole (VIII) which was isolated by centrifuging. After washing with acetone to remove any ammonium nitrate, the precipitate was dried at 0.1 mm over phosphorus pentoxide. The acid VI was then decarboxylated by heating its silver salt (VII) in a test tube, at  $250^\circ\text{C}$  in an oil bath (6). The product, 2-(p-nitrophenyl) osotriazole (VIII), derived from C-1 + C-2, distilled and crystallized out on the upper part of the tube. Its m. p. was in agreement with the reported value of  $183-184^\circ\text{C}$  (6).



This degradation has been carried out using non-radioactive glucose, but no difficulties are anticipated in applying it to the radioactive compound. The nitration is necessary because compound VIII without the nitro group is an oil, not as easily isolated or characterized as the crystalline derivative. In using radioactive glucose a barium hydroxide trap should be attached to the dry distillation of compound VII, the final step in degradation. Silver carbonate, formed in this reaction, decomposes at 218° C with liberation of carbon dioxide. The trapping and counting of this gas would confirm the radioactivity on C-3 of the glucose. Heating aqueous solutions in recrystallizations should be done under reflux because some osotriazole derivatives are volatile in steam. All compounds formed in this degradation are well characterized crystalline compounds, soluble in organic solvents such as chloroform, ethanol, pyridine and acetone.

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## The Adaptation of the Voges-Proskauer Reaction for the Quantitative Assay of Streptomycin

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At the present time there are several chemical methods for the assay of streptomycin. The principal chemical methods are the tests of Sullivan and Hilmer (1), Boxer, Jelinek, and Leghorn (2), and Marshall *et al.* (3). The test of Sullivan and Hilmer (1), is not sensitive with concentrations of the antibiotic lower than 1000 units/ml and values are high due to breakdown products formed during the test. The methods of Boxer, Jelinek, and Leghorn (2), and Marshall (3) are excellent chemical assay methods for streptomycin, but neither is adaptable to the assay of dihydrostreptomycin. All 3 of these assay methods require considerable time to perform.

The Voges-Proskauer reaction depends on the production of acetylmethylcarbinol or acetoin from glucose metabolism. In the presence of potassium hydroxide, acetylmethylcarbinol is oxidized to diacetyl which reacts with substances containing a guanidine residue to give a red-colored compound. Streptomycin

and dihydrostreptomycin both contain 2 free guanido groups, which might be expected to complete this reaction. The purpose of this paper is to report a modification of the Voges-Proskauer reaction that permits a rapid quantitative assay for either form of the antibiotic.

Modifications of the Voges-Proskauer reaction such as the methods of Harden and Norris (4), Barritt (5), O'Meara (6), and Coblenz (7) were investigated to determine their desirability for use in the assay of either form of the antibiotic. Acetylmethylcarbinol (Matheson Co.) was used for preliminary work but, because of its unstable nature, diacetyl (Eastman Distillation Products Industries) was later adopted as the reagent of choice. These various modifications of the Voges-Proskauer reaction were repeated many times, using varying amounts of reagents, different concentrations of reagents, and different sequences of addition of reagents. After optimum conditions had been determined, tests were carried out with different concentrations of streptomycin and dihydrostreptomycin to determine the sensitivity of the assay. Color readings were made with a Klett-Summerson photoelectric colorimeter using filters #42, 54, and 66.

Except for the modifications of Harden and Norris (4) and Barritt (5), all the procedures of the Voges-Proskauer reaction proved to be unsatisfactory because of lack of sensitivity. After modification of these 2 methods the following procedure was developed. The amounts and concentrations of reagents were placed in Klett-Summerson tubes in the following order.

Streptomycin (varying concentrations) —	1.0 ml
Alpha naphthol (5% in 95% ethanol) —	0.5 ml
Potassium hydroxide (40%) —	0.1 ml
Distilled water —	2.9 ml
Diacetyl (1:1000 dilution) —	0.5 ml

The function of potassium hydroxide in the Voges-Proskauer reaction is thought to be that of oxidation of acetylmethylcarbinol to diacetyl. Therefore, it would seem that if diacetyl were used, potassium hydroxide would not be needed. It was found that no color developed if potassium hydroxide was omitted. This indicates a new and unexplained function of potassium hydroxide in the reaction. It was found that the addition of streptomycin first and diacetyl last will give positive results whereas any other order of addition will give negative results. The tubes were shaken for 10 min to develop maximum color and then read for transmittency percentage in the colorimeter, using the #54 green filter. Maximum color was found to be stable for 15 min and tubes must be read within this time. In order to determine concentrations of streptomycin or dihydrostreptomycin greater than 1000 units/ml, 1.0-ml samples must be diluted to a total volume of 20.0 ml with distilled water, and sample amounts may then be assayed. Concentrations as low as 25 units/ml may be determined for either form of the antibiotic. This procedure gives a reproducible quantitative color test which fulfills Beer's law for any concentration from 25 units/ml to 1000 units/ml.



A standard curve can be developed by which unknown samples of the antibiotic may be assayed.

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## Liver Function and Bromsulfalein Disappearance<sup>1</sup>

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In the bromsulfalein test of liver function, a known amount of the dye (which is designated "BSP") is injected intravenously, and its subsequent concentration in the blood is measured after one or more selected time intervals. MacDonald published both normal and abnormal curves of BSP disappearance in humans (1). Before 1947 it was assumed that BSP disappearance from the blood is caused only by its removal in the liver and excretion in bile. However, in 1947, Cohn, Levine, and Streicher published the results of experiments with dogs that provide good evidence of extrahepatic uptake of BSP (2). Those results support the following approximate interpretation of the BSP disappearance curves.

Let  $y = y(t)$  and  $s = s(t)$  be the amounts at time  $t$  (in min) of BSP in the blood and in the extrahepatic, extravascular tissues, respectively. Assume that all rates of BSP transfer are proportional to the amount of BSP from which the transfer occurs. Let  $k_1$ ,  $k_2$ , and  $k_3$  be the proportionality constants for the transfers from  $y$  to  $s$ , from  $s$  back to  $y$ , and from  $y$  to the liver excretion, respectively. Then

$$\begin{aligned}\frac{dy}{dt} &= k_3 s - (k_1 + k_2)y, \\ \frac{ds}{dt} &= k_1 y - k_2 s, \\ s(0) &= 0, \text{ and } y(0) = y_0.\end{aligned}\tag{1}$$

This differential system has a solution of the form

$$y(t) = A e^{-r_1 t} + B e^{-r_2 t},\tag{2}$$

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<sup>3</sup> The author thanks Donald S. Amatusio for helpful discussions and for preliminary communication of experimental results being obtained by him and his associates at the Veterans Administration Hospital.

where  $-r_1$  and  $-r_2$  are roots of the algebraic equation in  $r$ ,

$$r^2 + (k_1 + k_2 + k_3)r + k_2 k_3 = 0,$$

and

$$A = (r_1 - k_2)y_0/(r_1 - r_2) \text{ and } B = (k_2 - r_2)y_0/(r_1 - r_2).$$

Also,

$$r_1 + r_2 = k_1 + k_2 + k_3 \text{ and } r_1 r_2 = k_2 k_3,$$

so that

$$k_1 + k_3 = (Ar_1 + Br_2)/y_0,\tag{3}$$

$$k_2 = (Br_1 + Ar_2)/y_0,\tag{4}$$

$$k_2 = r_1 r_2 / k_3 = r_1 r_2 y_0 / (Br_1 + Ar_2), \text{ and } k_1 = (k_1 + k_3) - k_2 = (Ar_1 + Br_2)/y_0 - r_1 r_2 y_0 / (Br_1 + Ar_2).\tag{5}$$

In applying these results to an experimental curve, it is first determined what values of  $A$ ,  $B$ ,  $r_1$  and  $r_2$  cause equation (2) to fit the experimental results. When the observed points are plotted on semilog paper the later portion, say for  $t > 30$ , is approximately linear and a measure of the term  $B e^{-r_2 t}$ —so this segment gives  $r_2$  from its slope and  $B$  as its extrapolation at  $t = 0$ . (For  $r_2$ , if  $y(t_1)$  and  $y(t_2)$  are on that segment and such that  $2y(t_2) = y(t_1)$  then  $r_2 = 0.693/(t_2 - t_1)$ . If the blood volumes is  $V$  in cc, if the dose is  $D$  in mg, and if  $y$  is measured in mg/100 cc of blood, then

$$A = y_0 - B = 100 D / V - B.$$

In some cirrhotics, for example, the blood volume is not given accurately by the usual tables relating blood volume to weight and height. In these cases  $A$  is determined more accurately from the quantity  $(y_0 - B)$  with  $y_0$ , being the extrapolation of the  $y(t)$  curve back to about  $t = 2$ , which allows a couple of minutes for the initial mixing after injection. (This extrapolation is best done on the semilog plot.) The value of  $r_1$  is determined in the same way as  $r_2$ , but from the best straight-line fit of the semilog plot versus time of the quantity (the observed value—the value of the above  $B e^{-r_2 t}$  at the time of the observation). With these observed constants one calculates the  $k$ 's by using equations (3), (4), and (5).

The initial slope on the semilog plot of the observed curve is a rough measure of  $k_3$ —especially if the dose is small and if the tested individual is normal in having a  $k_3$  that is large relative to  $k_1$  and  $k_2$ . According to this measure and MacDonald's results (1) the  $k_3$  values of normal individuals are between 0.14 and 0.4 when the dose is 2 mg/kg and between 0.075 and 0.25 when the dose is 5 mg/kg. The  $k_3$  values appear to be less in individuals with diseased or impaired livers— $k_3$  may even be as low as about 0.01 (Fig. 7, curve 7 of ref. 1).

In routine testing for impaired liver function it would be best to take measurements every 5 or 10 min for about half an hour and every 10 or 20 min for at least another half hour. This is recommended because in cases with impaired liver function the values of  $k_1$  and  $k_2$  may be greater than normal (possibly



due to some compensatory mechanism) and thus necessitate the determination of all the constants in equations (2) and (4). Such an analysis would require a minimum of 4 determinations, at about 3, 10 or 15, 30 or 40, and 60 or 80 min. In other words, the analysis of BSP curves for abnormals (mild or severe) is much more complicated than that of normal BSP curves if the results are to be equally accurate and clearly definitive. In case the above steps of the curve analysis are omitted or improperly done, the more likely error is the underestimation of the extent of liver impairment.

The present interpretation gives an approximate confirmation of Goodman's conclusions about normal cases, but his results for abnormal cases would sometimes be too high (3).

The present theory also applies to the hepatectomized dogs of Cohn, Levine, and Streicher (1). In that case  $k_2 = r_2 = 0$  and the last term of equation (2) is constant.

This treatment neglects the reabsorption factor described by Lorber and Shay (4). That factor should give rise to theoretically low values of  $k_2$  (and higher values of  $k_1$  and  $k_3$ ), but these would still be correct in regard to over-all physiological significance.

If  $E$  is the efficiency with which the liver removes BSP from the blood flowing through it, and if  $F$  is the fraction of the total blood volume that flows through the liver each minute, then  $k_2 = EF$ . Since  $0 < E < 1$  it follows that  $k_2$  is an upper limit for liver blood flow,  $F$ . However,  $k_3$  itself is the physiologically significant quantity, or measure, of this particular liver function.

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### The Influence of Iodoacetate on the Sodium and Potassium Content of *Ulva lactuca* and the Prevention of Its Influence by Light<sup>1</sup>

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The influence of glycolytic inhibitors on cation equilibria and movements in living cells has been investigated by Wildbrandt (1), Harris (2), and Maizels (3) on human erythrocytes, Dean (4) on

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<sup>2</sup> The authors wish to acknowledge the technical assistance of William De Witt Andrus.

muscle, Dixon (5) on brain cortex, and Scott *et al.* (6) on baker's yeast. An interpretation of the action of these agents has been based on their inhibitory effect on specific enzyme systems of carbohydrate metabolism which are associated with ion transport and equilibria.

The experiments to be reported represent a study of the influence of one of the glycolytic inhibitors, moniodoacetate, on the sodium and potassium content of the green alga, *Ulva lactuca*. The study was undertaken to test the applicability of the postulated role of glycolysis in cation regulation in this form.

The cells of this marine organism, like most cells living in a high  $\text{Na}^+$  low  $\text{K}^+$  medium, accumulate  $\text{K}^+$  and partially exclude  $\text{Na}^+$ . Since the alga consists of large membranous fronds of two layers of cells, it is particularly well suited for investigations involving ion interchange between the cell and its environment.

The *Ulva*, collected from the Eel Pond in Woods Hole, was conditioned before use under incandescent illumination in running sea water. Small uniform samples cut from a single frond were placed in large finger bowls of sea water, containing the inhibitor when present, and maintained in the dark or in the light at the temperature of running sea water (ca. 21° C). Samples were removed at various time intervals, rinsed for 1 min in isotonic sucrose (0.6 M) to remove adhering salts. The sucrose solution was then removed from the surface by a consistent blotting procedure. A wet weight was determined on the blotted material and, after drying for 12 hr at 110° C, a dry weight was taken. Cell water was calculated by difference. The dried material was ground in a mortar and extracted in 50.0 ml of 10% trichloroacetic acid for a few hours. The observation has been made in our laboratory that  $\text{Na}^+$  and  $\text{K}^+$  are quantitatively extracted from the material by this method as compared with the usual wet ashing techniques. The extracts were analyzed for  $\text{Na}^+$  and  $\text{K}^+$  by flame photometry, using the Beckman spectrophotometer.

*Influence of sodium iodoacetate on cellular potassium in the dark and in the light.* The presence of the inhibitor in a concentration of 0.001 M results in a marked loss of  $\text{K}^+$  from the cells over a period of 24 hr in the dark. Control samples taken at the beginning and end of this period were essentially constant in potassium content (Fig. 1). In the presence of light from a 100-w incandescent lamp placed at a distance of about 1 ft from the alga, the inhibitor is completely ineffective in causing loss of  $\text{K}^+$ . Rather, the potassium content of the experimental materials temporarily increases over that of the controls.

To evaluate further the influence of light on the prevention of the iodoacetate effect, the concentration of the inhibitor was raised to 0.005 M. Again the light prevented the loss of  $\text{K}^+$  (Fig. 1).

*Influence of sodium iodoacetate on cellular sodium in the dark and in the light.* Concomitant with the  $\text{K}^+$  loss caused by the 0.001 M  $\text{NaIAA}$  in the dark the



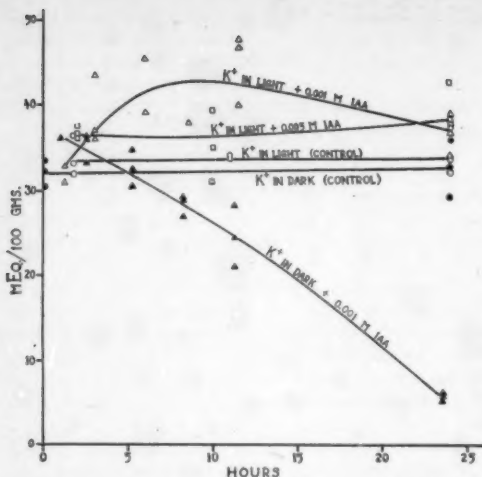


FIG. 1. The influence of moniodoacetate on the potassium content of *Ulva lactuca* in the light and in the dark. Potassium is expressed in terms of cell water.

cellular sodium increases over that of the controls, although the condition of darkness alone is sufficient to cause some sodium increase. Illumination again prevents this action of the inhibitor, and the sodium is actually somewhat reduced compared to the controls (Fig. 2). Light also prevents an increase in sodium when the inhibitor concentration is raised to 0.005 M.

An examination of a large body of unpublished data indicates a close correlation between potassium content and calculated cell water in *Ulva lactuca*, while sodium content is most consistent on a dry weight basis. For these reasons, the potassium and sodium data are expressed as indicated, although essentially the same results appear when the data for each ion are expressed on either basis. These observations may reflect a largely ionized cellular potassium and a partially bound sodium. Confirmatory evidence for the ionized state of potassium has been recently obtained in our laboratory by experiments with  $K^{42}$  which indicate that all the potassium in the cell is readily exchangeable (7).

The normal variation in potassium content encountered in samples from different fronds or in different samples from the same frond, probably a reflection of varying physiological conditions within the cells, is usually accompanied by a reciprocal sodium variation.

Iodoacetate, in low concentrations, has been shown by experiments *in vitro* to inhibit selectively glyceraldehyde dehydrogenase, one of the glycolytic enzymes (8). It has been proposed, since iodoacetate caused a loss of  $K^+$  from erythrocytes, muscle, brain cortex, and yeast cells, that the normal accumulation of this cation is dependent on the intact glycolytic system (3-6). The additional observation by Maizels (3) of a gain of  $Na^+$  by human erythrocytes in the presence of the inhibitor suggests an active sodium extrusion

process dependent on glycolytic energy. The interpretation of the action of iodoacetate in the dark in causing a loss of  $K^+$  and a gain of  $Na^+$  in *Ulva lactuca* is consistent with this hypothesis.

The prevention of these ion shifts by light lends further support to this hypothesis, since phosphoglyceric acid, the compound which is formed by the action of glyceraldehyde dehydrogenase, has been shown by Calvin and Benson (9) and confirmed by Fager and Rosenberg (10) to be the first stable product formed in the photosynthetic reduction of carbon dioxide. Hence, in the light, even in the presence of the inhibitor, which prevents the glycolytic formation of phosphoglyceric acid, this intermediate is made available to cellular metabolism by photosynthesis. The above evidence suggests, therefore, that the normal  $Na^+$  and  $K^+$  distribution in this organism depends on the utilization, in some way, of phosphoglyceric acid. The degradation of this compound could provide energy for synthetic processes maintaining the normal constituents of the plasma membrane, thus affecting the permeability *per se* of the cell for cations. This phase of cation regulation has been particularly emphasized by Parpart and Green (11) in relation to factors affecting the  $Na^+$  and  $K^+$  balance in the erythrocyte. Since iodoacetate inhibits glycolytic synthesis of adenosinetriphosphate, another interpretation for these results might be that ATP ions, which according to a novel hypothesis proposed by Ling (12), "when absorbed on proteins could supply a strategically indispensable part of the fixed charges which would selectively attract  $K^+$  and displace  $Na^+$  from the cell."

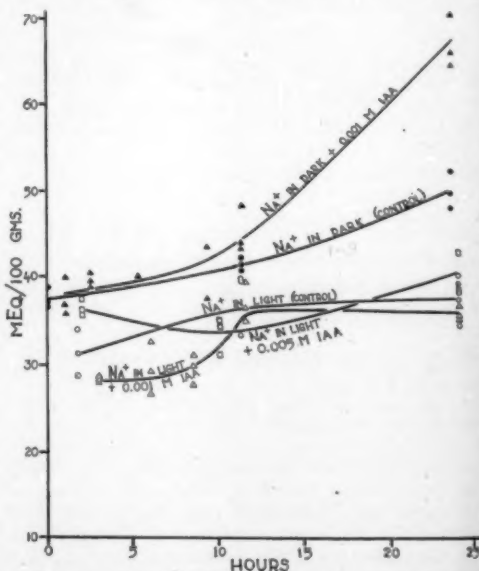


FIG. 2. The influence of moniodoacetate on the sodium content of *Ulva lactuca* in the light and in the dark. Sodium is expressed in terms of dry weight.

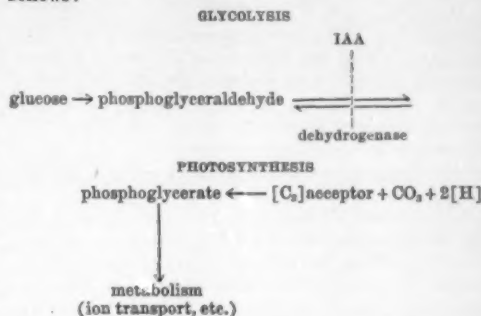


In the opinion of the authors, however, a more probable explanation of the observation here reported, and a view favored by further investigation of the problem in this organism (13), is as follows: Ion transport mechanisms, as yet to be elucidated, would be necessary to compensate for the continual flow of these cations with their concentration gradients across the cell surface. Such transports, according to this interpretation, would be energized by the metabolic degradation of phosphoglyceric acid, perhaps through the mediation of high energy phosphate bonds as in ATP.

A further elucidation of the precise mechanisms involved in this problem will pertain to one of the most fundamental activities of living cells: the capacity to maintain within cell boundaries a chemical composition which is characteristically different from that of the external environment, and here particularly

the ability to concentrate  $K^+$  and partially exclude  $Na^+$  against their respective concentration gradients.

The postulated reactions may be summarized as follows:



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Manuscript received November 6, 1952.

## Association Affairs

### Southwestern Division Meeting

Frank E. E. Germann, *Secretary*

#### Southwestern Division

THE Southwestern Division of the AAAS held its twenty-ninth meeting in Tempe, Arizona, during the week of April 19th on the campus of the Arizona State College. One hundred and eighty persons registered, although the number participating in the meetings was much larger than this. As usual, many students took advantage of the opportunity to attend a regional scientific meeting. The sessions opened with a meeting of the Executive Committee, on which occasion John A. Behnke, Associate Administrative Secretary of the AAAS, represented the Washington office. At this time Wyoming and Montana East of the Continental Divide were officially added to the Division. Mr. Behnke reported briefly on the activities in the Washington office, as well as concerning the annual meetings scheduled for Boston and San Francisco.

In addition to the regular programs of sections, two special symposia were presented.

#### CONSERVATION SYMPOSIUM

Martin Mortensen, *Presiding*

1. The Nature of Conservancy in Arizona. Lealie N. Goodding, St. David, Arizona.
  2. The Status of Conservation Teaching in New Mexico. Howard J. Dittmer, University of New Mexico, Albuquerque.
  3. Report on Conservation Education Project Activities in Arizona. Wayne Kessler, Assistant State Conservationist, State Land Department, Arizona.
- A summary of activities involving conservation education projects, in the following subdivisions: (1) in public schools, including high schools and grammar schools; (2) in the Arizona Conservation Districts; (3) in connection with cooperative agencies from the federal, state, and local governments.
4. General Discussion by Panel, led by Chairman Mortensen.

#### DESERT AND ARID ZONE SYMPOSIUM

Peter C. Duisberg, *Presiding*

1. Committee Accomplishment, 1952-53. Victor Schoffelemaier, Glendale, California (Former President, Texas Chemurgic Council).
2. Survey of Desert and Arid Zone Research in Progress in the Southwest. E. J. Workman, President, New Mexico Institute of Mining and Technology, Socorro.



3. Worldwide Efforts Toward Arid Zone Research. Peter C. Duisberg, Desert Products Company, El Paso.

4. Committee Suggestions for Further Activity. Herbert L. Stahnke, Arizona State College, Tempe.

5. General Panel Discussion.

Other special features were the annual Powell Lecture in honor of the explorer of the Grand Canyon, given by Emil W. Haury of the University of Arizona on the subject "Dating of Early Man," and an illustrated talk on "Desert Denizens" by Herbert L. Stahnke.

The General Session on April 22 adopted the following resolutions:

1) "In order to increase both the membership and the effectiveness of the AAAS, its Southwestern Division requests the Board of Directors of the AAAS to explore possibilities of additional types of membership. Examples of these types are student membership, memberships without journal subscriptions, two memberships (such as man and wife) in one family, and emeritus status. If the study results in new action, it should be appropriately publicized, preferably by publication in *SCIENCE*.

2) "Resolved that the Southwestern Division of the AAAS instruct its Desert and Arid Zone Committee to explore the possibility of cooperating with UNESCO to the end of bringing an International Desert Symposium to the Southwest.

3) "Resolved that the Desert and Arid Zone Committee be instructed to study the possible sources of funds to stimulate and aid in sponsoring Arid Zone Research.

4) "It is the considered opinion of this Division of the AAAS that the challenging possibilities of television as an educational factor of the first order be used increasingly to acquaint the public, and espe-

cially the younger generation, with the progress and achievements of science.

"For the fullest implementation of such science education via television we feel that educationally owned and operated television stations are essential, and should be encouraged in every way.

"The Southwestern Division of the AAAS therefore resolves that it wholeheartedly favors, and will encourage and support, the development in the Southwest of television stations on these channels in this area reserved by the Federal Communications Commission for educational work."

New officers elected were Herbert L. Stahnke of the Arizona State College at Tempe, President, and Joe Dennis of the Texas Technological College, Vice President. Frank E. E. Germann, of the University of Colorado remains Permanent Secretary. E. J. Workman of the New Mexico Institute of Mining and Technology, and Alan T. Wager of the Arizona State College of Tempe were elected to the Executive Committee. George M. Bateman of the Arizona State College at Tempe, James A. McCleary of the Arizona State College at Tempe, W. J. Coster of the University of New Mexico, and W. C. Holden of the Texas Technological College at Lubbock were chosen Chairmen of the Physical, Botanical, Zoological, and Social Science sections respectively. Bartlett Dewey of the Eastern New Mexico College and William M. Pierce of the Texas Technological College were elected secretaries of the Physical and Social Sciences sections respectively, and Edwin R. Helwig of the University of Colorado will continue as secretary of both the Botany and Zoology sections.

Future meetings are scheduled as follows: 1954, Lubbock, Texas; 1955, Santa Fe, New Mexico; and 1956, Las Cruces, New Mexico.

## Scientific Book Register

*Modern College Physics*. 2nd ed. Harvey E. White. New York-London: Van Nostrand, 1953. 823 pp. Illus + plates. \$6.75.

*Robert Grosseteste and the Origins of Experimental Science, 1100-1700*. A. C. Crombie. New York: Oxford Univ. Press, 1953. 369 pp. Illus. + plates. \$7.00.

*Introduction to Exceptional Children*. Rev. ed. Harry J. Baker. New York: Macmillan, 1953. 500 pp. + plates. \$5.00.

*The Zoological Record*, Vol. 87. Records of zoological literature relating chiefly to 1950. G. Burder Stratton, Ed. London: Zoological Society, 1953. 19 sections. £6 for complete volume with special prices for separate sections.

*Oxidation of Metals and Alloys*. O. Kubaschewski and B. E. Hopkins. New York: Academic Press; London: Butterworths Scientific Pubs., 1953. 239 pp. Illus. \$6.00.

*Africa: A Study in Tropical Development*. L. Dudley Stamp. New York: Wiley; London: Chapman & Hall, 1953. 568 pp. Illus + maps. \$8.50.

*Starch: Its Sources, Production and Uses*. Charles Andrew Brautlecht. New York: Reinhold, 1953. 408 pp. Illus. \$10.00.

*Inorganic Thermogravimetric Analysis*. Clément Duval. Amsterdam-Houston: Elsevier, 1953. 531 pp. Illus. \$11.00.

*Kiva Mural Decorations at Awatovi and Kawaika-A*. With a survey of other wall paintings in the Pueblo Southwest. Papers of the Peabody Museum of American Archaeology and Ethnology, Vol. XXXVII. Watson Smith. Cambridge, Mass.: Peabody Museum, Harvard University, 1952. (Published with the assistance of the Wenner-Gren Fdn. for Anthropology). 363 pp. Illus. + plates. \$10.00; paperbound \$7.50.

*Animal Micrology*. Practical exercises in zoological micro-technique. 5th ed. Michael F. Guyer; with a chapter on drawing by Elizabeth A. Bean. Chicago: Univ. Chicago Press, 1953. 327 pp. Illus. \$4.75.

*An Introduction to Statistical Science in Agriculture*. D. J. Finney. Copenhagen: Ejnar Munksgaard; New York: Wiley, 1953. 179 pp. Illus. \$3.75.



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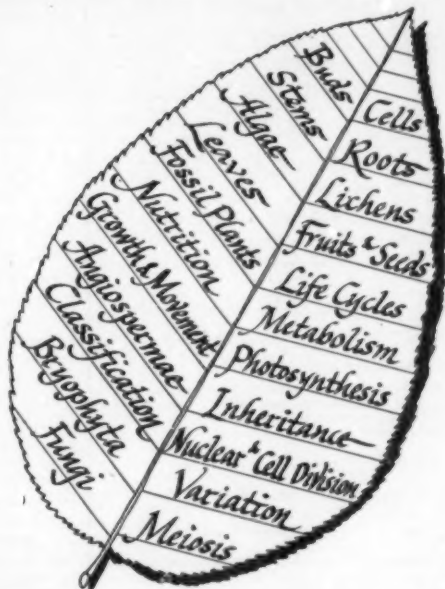




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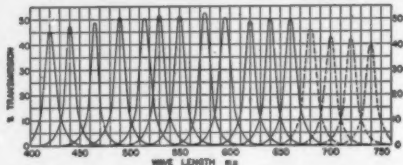
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## Meetings & Conferences

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June 29-July 3. American Society for Testing Materials. Chalfonte-Haddon Hall, Atlantic City, N. J.

July 1-3. American Physical Society. Fluid Dynamics Division. Pennsylvania State College, State College, Pa.

July 5. Colloquium on Cosmic Rays. Bagnères-de-Bigorre, France.

July 6-11. Symposium on Gas Dynamics of Interstellar Clouds. Cambridge, England.

July 7-8. Society for the Study of Fertility (4th Annual). Liverpool.

July 7-9. Ciba Foundation Symposium on the Kidney. London.

July 7-9. Research Conference on Female Reproduction in Farm Animals. Iowa State College, Ames, Ia.

July 12-16. Congreso Panamericano de la Prensa Medica, and Semana de Alta Cultura Medica Europea. Buenos Aires.

July 13. International Astronomical Union, Symposium on Hydrodynamics of Gaseous Masses. Cambridge, England.

July 13-17. British Medical Association (Annual). Cardiff, Wales.

July 14-25. International Congress of Radiologists (6th). Copenhagen.

July 17-19. California and American Federation of Mineralogical Societies, San Diego, Calif.

July 18. American Mathematical Society (58th Summer Meeting). Kingston, Ontario.

July 18. Conference on Ionisation Phenomena in Discharges. Oxford, England.

July 19-26. Congress of the Latin American Society of Orthopaedics and Traumatology (2nd). Rio de Janeiro.

July 20-23. American Veterinary Medical Association. Toronto.

July 20-25. International Congress on Medical Librarianship. London.

July 24-25. Physiological Society Meeting. Cambridge, England.

July 25-28. International Committee of Electrochemical Thermodynamics and Kinetics (5th Annual). Stockholm, Sweden.

July 26-30. International Psychoanalytical Congress (28th). London.

July 26-31. International Congress of Gynaecology and Obstetrics. Geneva.

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July 29-Aug. 4. International Congress of Pure and Applied Chemistry and International Union of Pure and Applied Chemistry. Stockholm.

July 30-Aug. 1. Wyoming Geological Association. University of Wyoming, Field Conference. Laramie.

Aug. 3-5. Abnormal and Pathological Plant Growth. Brookhaven National Laboratory, Upton, L. I., N. Y.

Aug. 3-8. Photographic Society of America. Los Angeles, Calif.

Aug. 5-12. International Congress of Zoology. Copenhagen.

Aug. 10-14. Society of American Bacteriologists (Annual). San Francisco.



# The Wiley Bulletin

SCIENCE EDITION

New York

June 26, 1953

## THE PLACE OF THE PREFACE IN CHOOSING A TEXTBOOK



Often the Preface is the true key to the book. Not only does it explain the reasons for writing that particular book, but it gives pertinent information on the scope intended, the viewpoint, the approach, and, equally important, the limitations imposed by the author. Failure to fully appreciate this last can often result in a misconception on the part of the reader. Faced with a choice between intensive treatment

of a very limited field or a less complete coverage of a wider area, each author selects the type of coverage which will best accomplish his aim.

In the Preface of "General Physiology" Bradley T. Scheer of the University of Oregon explains his choice of the latter treatment: "... because I believe that the consistent viewpoint thus developed is worth the necessary sacrifice." The wide coverage of the work is in keeping with the author's avowed aim, which is also stated in the preface: "... a thorough first course in physiology which will provide an intelligible, up-to-date picture of vital functions, shorn of as much irrelevant detail as possible, yet offering a clear exposition of the nature and present status of the basic problems of physiology."

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## STRUCTURE OF PERSONALITY STUDIED

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The book will be published in this country soon with approximately 241 pages and at a probable price of \$6.00.

## WILEY AUTHOR WINS HARVARD PRIZE

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The book deals with the when, why, and how of nationalism, offering a structural and quantitative analysis which paves the way for eventual measurement and prediction in this field. It is the first book to apply some of the new ideas of communication theory to the fundamental problem of nationalism, and to suggest ways in which these ideas may be usefully combined with other social science methods. The results of the analysis are presented against a background of empirical and statistical data drawn from the world over.

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Russian Contribution to Soil Science	J. S. Joffe	New Jersey Agricultural Experiment Station Rutgers University
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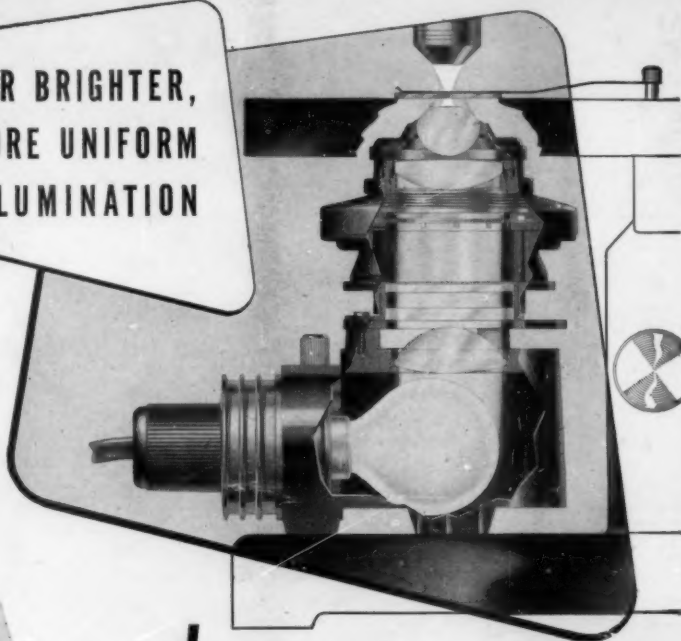
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